

Thesis submitted for the degree
of Ch. M. Edinburgh.

by

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1929

THE DEVELOPMENT (prenatal) OF THE FEMALE GENITAL TUBE.

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NOTE.

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I should like to express here my indebtedness to the Trustees of the William Gibson Research Scholarship, under the auspices of which a considerable part of the work embodied in this thesis has been done.

I also wish to say how grateful I am to Professor J. Ernest Frazer, in whose laboratory the work has been carried out, and who has helped me so much with advice, and criticism, as well as with practical assistance and permission to use his valuable specimens.

THE DEVELOPMENT OF THE FEMALE GENITAL TUBE.

Scope of Paper.

Before commencing a detailed study and description, it will be well to define the scope of what is intended in this paper. Much work has been done in the past on the development of the various portions of the Female Genital Tube, but the study has tended, in individuals, to be markedly specialised and limited to one small stage of growth or portion of this tract, and in this way the correlation and sequence of development, between various parts and stages, has been, perhaps, a little obscured.

In this paper, it is intended to trace the development of the Female Genital Tube - that is the Fallopian Tube, Uterus, Cervix, Vagina, and Hymen, from the earliest to the fully developed stage, following out the description, step by step, in the various embryos of which we have specimens. In this way it is hoped to synchronise and correlate various stages of development and, by adding short summaries of the consecutive development of each portion of the female genital tract, to obviate or minimise any confusion which might arise.

INTRODUCTION.

While it is not possible to attempt a description without mentioning and, to a certain extent, describing these structures with which the Genital Tube is so closely allied - viz. the Wolffian Duct and gland, no detailed study of these will be undertaken here.

In their origin, and throughout their - specially early - development, the excretory and genital systems are so closely allied, that no adequate description of the latter can be undertaken without some preliminary description of the former.

In common with most vertebrates, the development of the human excretory system is a gradual one. In man and the higher forms the evolutionary stages are three in all - pronephros, mesonephros and metanephros - the metanephros being formed last and being retained as the functional kidney. This development only differs in degree from that of more primitive forms. The most primitive develop only to the pronephros, which is retained as the permanent, functional, excretory organ, while more developed forms reach the second or mesonephros stage.

In man the pronephros no longer functions as an excretory organ, and its development is therefore rudimentary and abbreviated and need not concern us here. The metanephros, becoming the true functional kidney, belongs to a different course of investigation.

GENERAL DESCRIPTION OF GENITAL ORGANS & MESONEPHROS.

In its origin and throughout its early development, the Female Genital Tube is closely concerned with the mesonephros, and a consideration of this structure, in its topography and connections can, with advantage, be taken up here.

To quote from Felix(1)- "The Mesonephros is formed along the posterior wall of the body cavity. Only at the very beginning of its development does it find sufficient space in the retroperitoneum; as soon as it begins to expand, it needs more room, and this it finds in the direction of the body cavity, invaginating the coelom wall as a fold into this.

"This fold, later, contains also the Müllerian Duct, and reproductive gland, in addition to the mesonephros, and is therefore termed the urogenital fold." It becomes divided throughout its entire length, with the exception of the cranial and caudal ends, into a genital and a mesonephric portion.

"The Mesonephric fold, separated from the urogenital, becomes further subdivided in correspondence with its contents. Proceeding medially from the lateral surface, one meets in it the Müllerian Duct, the excretory (Wolffian) duct and the convolutions of the mesonephric tubules. The fold forms first a portion for the Müllerian Duct, the tubar² portion, then a common portion for the excretory duct and mesonephric tubules - the gland portion, and finally a thread-like connection with

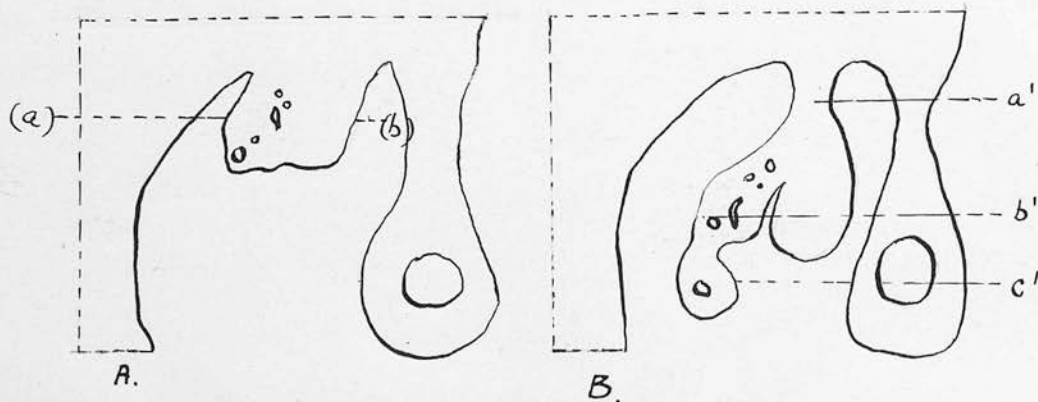


Fig. 1. Semischematic diagram to show A. mesonephros dividing into mesonephric (a) and gland portion (b) and B. Mesonephric fold dividing into tubar portion (a'), gland portion (b') and mesentery portion (c')

the posterior abdominal wall - the mesentery portion.

(See Fig. 1.)

"The tubar and gland portions regularly become separated by a slight furrow that sinks in from the lateral surface; the gland portion passes over gradually into the mesentery portion.

- - - - "In the female, the tubar portion contains only the Müllerian duct; in the male, it contains both Müllerian and excretory ducts. - - - The formation of the various portions begins at the cranial pole, and proceeds caudally, and the lateral portions are formed earlier than the medial ones. - - - The separation of the tubar portion begins in embryos of 13 mm. and it is the most freely mobile portion of the mesonephric fold.

- - - - "Originally the urogenital folds lie parallel with the vertebral column ... but as soon as the development of new organs - suprarenals, then metanephroi - begins between them, they - the urogenital folds - are displaced outwards, this being allowed for by an increased broadening of the posterior body wall and an increase in frontal diameter of the body cavity.

"Caudal to the metanephros, the enlarging force ceases and therefore the urogenital folds are not displaced. This displacement above, and absence of it below, produces a bend of the fold which is double in character, having an upper and lower sagittal, and a middle transverse portion."

Pari passû with the growth of the suprarenals and metanephroi, "the upper sagittal portion of the fold

comes to assume a more and more oblique position. The mesentery of the genital fold which is only fully formed in the upper sagittal portion necessarily assumes this oblique position and gains therefrom a great mobility." The Wolffian duct lies in the inner part of the fold, external to the Wolffian Body and extends from just near to the septum transversum of diaphragm to end by opening laterally into the ventral cloaca.

In the caudal sagittal portion - - - "the two folds come together and fuse, and by this fusion, a frontal partition is formed which divides the primitive pelvis into a dorsal and ventral half. This frontal partition forms the genital cord. It fuses with the floor of the body cavity, and the partition is thus a complete one."

We have, in the above description, seen the relation of the various portions of the mesonephros, etc., to each other and the embryo in general, and in so doing, have established a terminology and various points from which to work, and can now therefore commence the detailed study of the early development of the Female Genital Tube.

Before however, taking up the detailed study of the Female Genital Tube proper, I think it will be well to pause here and consider a particular part of it, not present as such in the adult, but of very great importance in the embryo - the Urogenital Sinus.

As the development of - especially - the lower end of the female genital tube is so closely bound up with the sinus, it will be necessary for a right understanding, I think, to trace in some detail, the formation of this structure, and the gradual changes in the relations of its component parts to each other.

The Early Development of the Urogenital Sinus.

Quoting Felix, in Keibel and Mall, (1A) "the rectum, bladder, urethra and urogenital sinus are formed by a triple division of the cloaca. The first division completely separates the dorsal third of the cloaca or rectum and the remains of the cloaca are divided by a second incomplete division into bladder, urethra and urogenital sinus.

- - - -"By cloaca is understood the part of the posterior intestinal bay, that lies caudal to the point where the allantois is given off. Into it there opens from above the hind gut and the allantois.

"It is a blind sac, oval in transverse section, its longest axis being sagittal and its ventral surface being compressed almost to an angle. By this ventral angle, the cloaca comes into contact, and fuses with the ectoderm of the surface of the body, the mesoderm

being pressed aside. This area of fusion is termed the cloacal membrane.

- - - - "The first division of the cloaca begins in embryos about the 5.3 mm stage; it separates a dorsal third or quarter (the rectum), and an anterior two thirds communicating with the allantois (the ventral cloaca), by means of a saddle or partition which grows downwards from above into the lumen of the cloaca - this partition being termed the septum urorectal." This urorectal septum grows down to reach the cloacal membrane and fuses with it, so that we can now speak of two divisions of this latter - - - "the anal membrane, which closes the rectum, and the urogenital membrane, which closes the ventral remains of the cloaca. In later development both membranes are broken through independently and so the urogenital and anal openings are formed." Thus, the urogenital and anal openings are not only distinct in formation, but widely separated from each other in the times at which they become patent. The breaking through of the urogenital sinus takes place from the 13 mm - 15 mm stage, whereas that of the anus is much later and very variable.

While the division that separates the rectum from the ventral remains of the cloaca is still progressing, the second division which divides the ventral remains of the cloaca into bladder, urethra and urogenital sinus is beginning.

The exact details of this division and change of form do not concern us here. It is sufficient to say that this ventral division of the cloaca is sub-

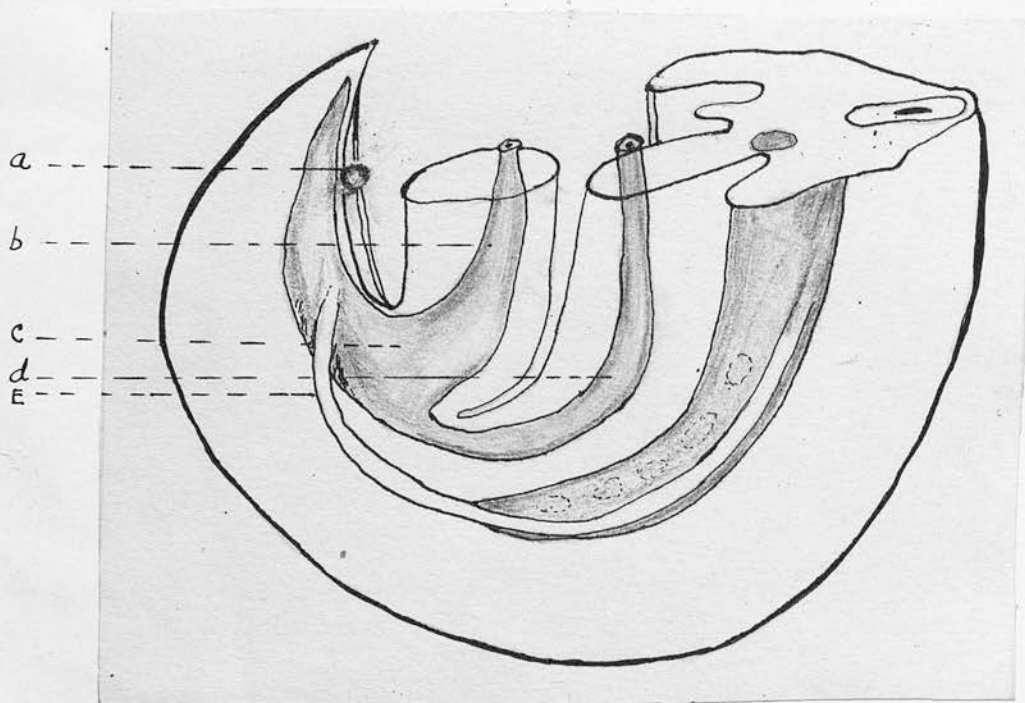


Fig. 2. 5.3 mm. embryo x 50. Reconstruction of hinder end (a) = Cloacal membrane (b) = Allantois (c) = cloaca. (d) = hindgut (e) = primary excretory duct.

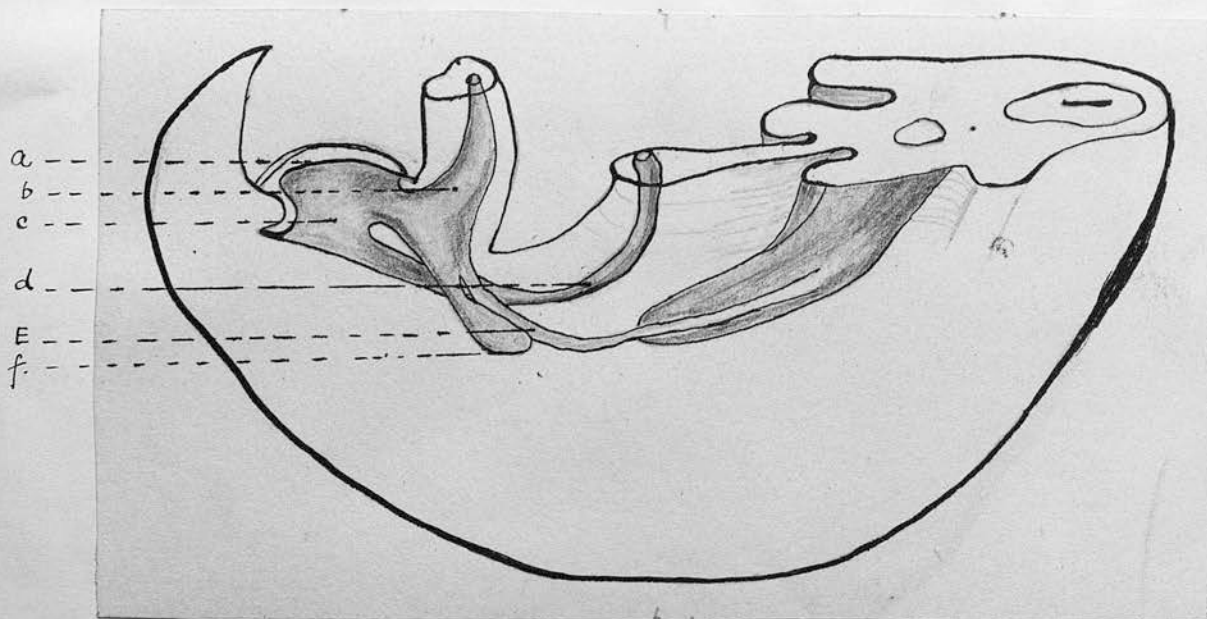


Fig. 3. 8.5 mm. embryo x 50. (a), (b), (c), (d), (e), as above (f) = ureteric bud.

Sam. J. Murthuman

divided into three portions by the depression of its anterior or ventral wall. From the posterior broad lumen the vesico-urethral anlage is formed - the narrow middle portion becomes the pars pelvina, and the broad ventral portion the pars phallica of the urogenital sinus.

The development of the bladder does not come in to this present study.

The primary excretory ducts open into the cloaca, (afterwards the pars pelvina of the sinus) at a very early stage. Later the Müllerian ducts reach the sinus lying between the Wolffian ducts and causing a projection of the posterior sinus wall - now termed the Müllerian tubercle.

The accompanying reconstruction diagrams (see Figs. 2 and 3) of the early development of the sinus in a 5.3 mm and 8.5 mm embryo need little explanation - and the further changes in the sinus will be described as they occur.

We are now in a position to commence a detailed study of the development of the Female Genital Tube.

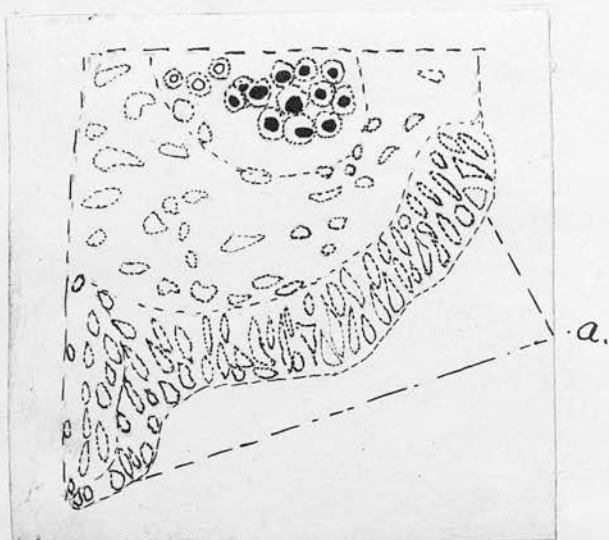


Fig. 4. 10 mm. embryo x 320 (a) = Early "Funnel area!"

The Ostium Abdominale & Early Development of the Müllerian Duct.

The Müllerian Duct arises as an invagination from the coelomic cavity of the epithelium covering the urogenital fold, the summit portion of which prepares itself for the reception of the tube, by beginning to project somewhat from the rest of the fold to form the tubar mesentery as described before. The area of epithelium in the fold, which is invaginated to form the ostium abdominale - is termed the "Funnel Area."

10 mm. Embryo. I have first been able to pick up this area in the 10 mm embryo in which it appears about the level of the third thoracic segment, as a circumscribed area of thickening, covered by rather tall columnar epithelial cells. (See Fig. 4.) There is here no true duct formation, but the whole area, which lies caudal to the cranial end of the urogenital fold, and on its ventro-lateral aspect, is slightly depressed.

12 mm. Embryo. In the 12 mm embryo, the funnel area is well marked, and present at about the level of the 5th - 6th thoracic segment. It lies immediately caudal to the dorsal limit of the pleuro-peritoneal membrane at the opening of the pleuro-peritoneal duct into the peritoneal cavity.

The funnel area here presents a deep groove, extending ventro-medially into the outer surface of the urogenital fold (Wolffian ridge), and thus coming to possess a dorsal and medial lip, which fuse to form a

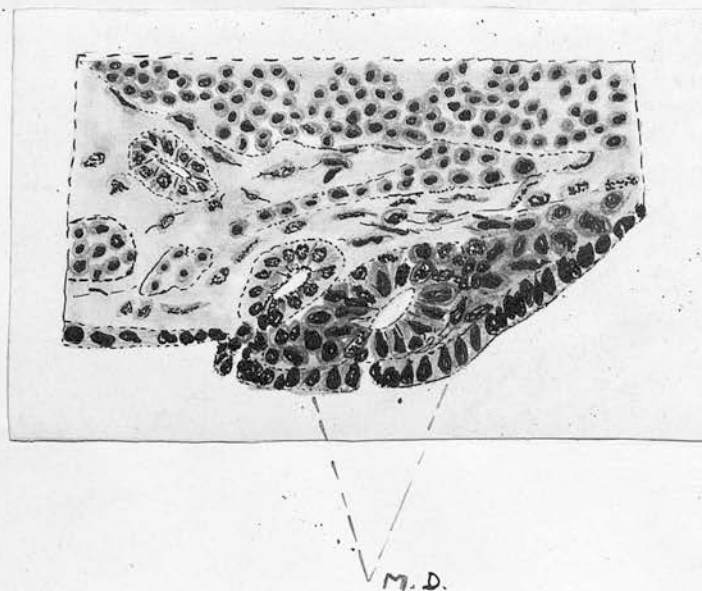


Fig. 5. 12 mm. embryo x 320 M.D.= formation of Müllerian duct by union
 2 of dorsal and medial lips

round duct. (See Fig. 5.) This round duct - The Müllerian tube - is lined by high columnar epithelium and, shortly after its completion, by loss of continuity with the surface epithelium, it terminates by becoming solid, in contact with the outer side of the Wolffian duct, having extended over only about some 8-10 (10u) sections. This completes the anlage of the cranial portion of the Müllerian duct.

To quote Felix (1B) - "When fully formed, it - (i.e. the anlage of the cranial portion of the Müllerian duct) - is cornet-shaped, the opening of the cornet corresponding to the cranial portion of the groove which remains open, while its tip corresponds to the closed portion, separated from the coelomic epithelium; the opening of the cornet into the abdominal cavity is termed the ostium abdominale tubae. The separated apex of the cornet lies in the immediate neighbourhood of the primary excretory duct, between it and the coelomic epithelium; it has, however, no connection with either!"

13 mm. Embryo. The funnel area is here very well marked, and lies at the level of the 6th thoracic segment. It is deeply grooved, the groove possessing well-defined ventral and dorsal lips, and looking dorso-laterally. The ventral lip inclines posteriorly towards the dorsal lip, and assuming a rather hooked outline, joins the latter, to form a well-marked rounded tube. On the original funnel area, which extends over the whole external and cranial tip of the Wolffian ridge, two other lesser

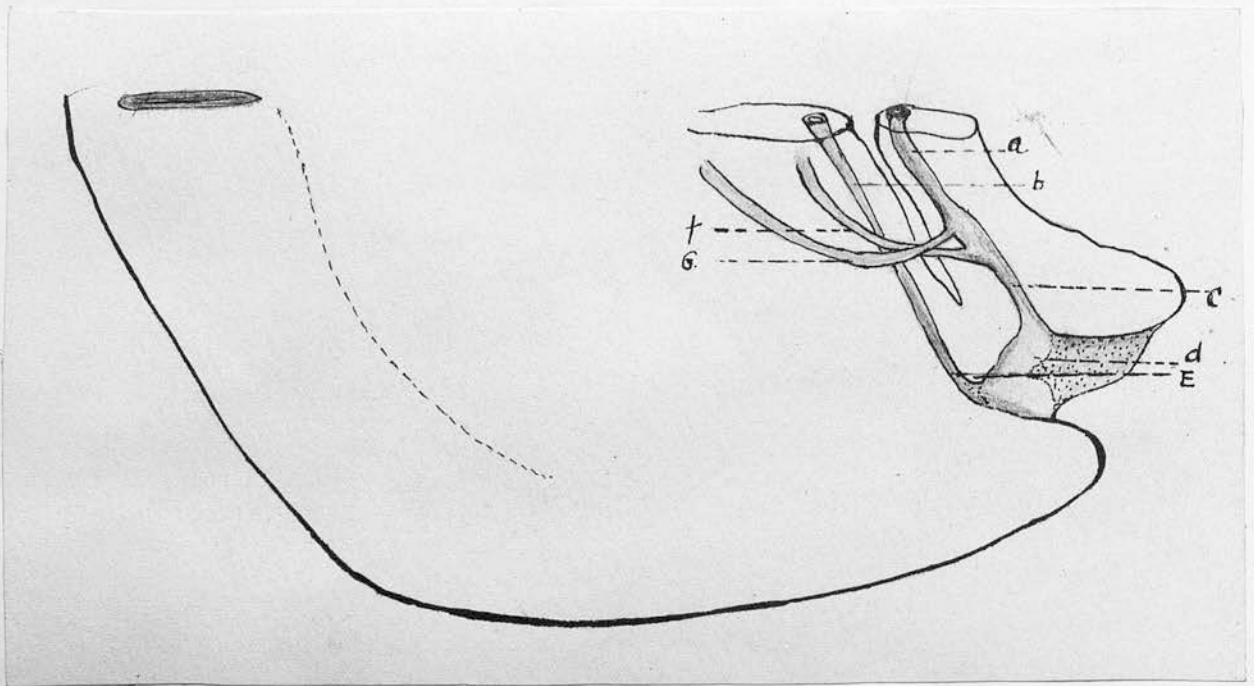


Fig. 6. 13 mm. embryo x 50. (a) = allantois (b) = rectum (c) and (d)
 = pars pelvina and pars phallica of sinus (e) = anal opening (f)
 = Wolffian duct (g) = ureter.

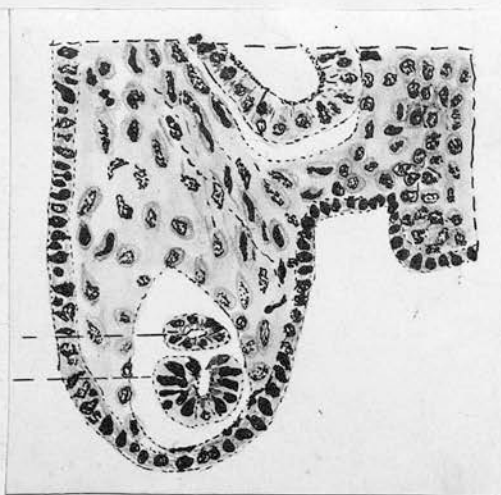
grooves can be detected, one ventral, which fuses with the base of the original ostium abdominale, before the lips of the latter have fused to form a closed tube, and one lateral, which fails to reach the lumen of the future Müllerian duct. The former of these - at least - forms an extra abdominal ostium, and together with the latter, outline the first anlage of the tubal fimbriae.

The Müllerian duct here persists as a well-marked rounded tube, lined by high columnar epithelium - over some 24-26 (10u) sections, and terminates by becoming solid, applied to the ventro-lateral aspect of the Wolffian Duct at the level of the 6-7th thoracic vertebra.

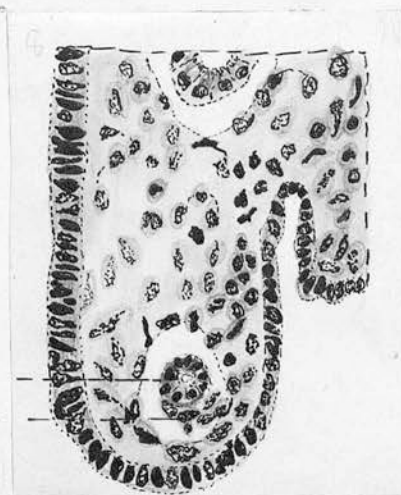
Sinus 13 mm. The division of the ventral portion of the cloaca by depression of its ventral or anterior wall into urethro-vesical anlage, pars pelvina pars phallica of the urogenital sinus is beginning but there is as yet no very definite differentiation of the three parts.

Both ventral and dorsal divisions of the cloaca now open to the exterior, but still by means of a common cloacal depression, the anterior part of which forms the commencing pars phallica of the urogenital sinus. The funnel-shaped depression in the wall of the urethro-vesical portion of the ventral cloaca, described in the last specimen, has become flatter, and the commencing differentiation of the openings of ureter and primary excretory duct is now taking place. (See Fig. 6.)

WD ---
MD ---



WD ---
MD ---



Figs. 7 & 8. 15 mm. embryo x 320. Termination of Müllerian duct (M.D.) by flattening out on surface of Wolffian duct = (W.D.).

a ---
M.D.o ---
a' ---

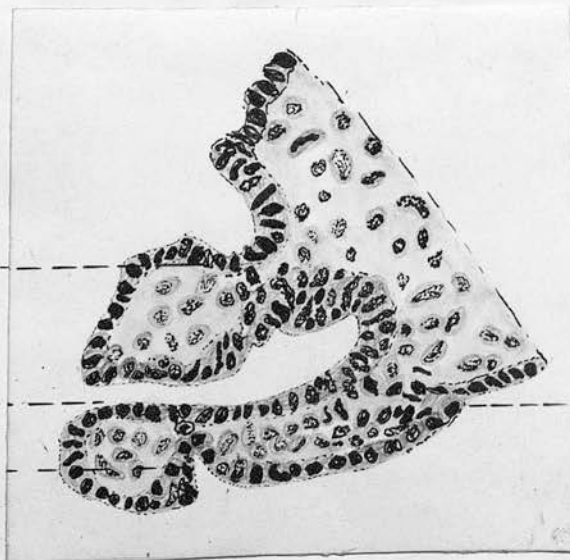


Fig. 9. 16 mm. embryo x 320 abdominal ostium of Müllerian duct = O.M.D. with accessory ostia (a), (a').

The genital tubercle is present and the lumen of the allantoic stalk is narrowing.

15 mm Embryo. In this specimen, the "funnel area" lies at the level of the 8th and 9th thoracic vertebrae, and possesses well marked dorsal and ventral lips, the ventral lip being the more prominent and better marked. Near the site of the original funnel area, minor "funnel areas" arise, at first as small solid cords of cells from a superficial surface depression, which later develop lumina and fuse with the Müllerian duct after this has become a completed tube. In this specimen, two or three of these accessory abdominal ostia can be made out.

Note. I have not, in any of my specimens, been able to make out accessory tubes as described by Felix, (1C.) These can, according to this author, be distinguished from accessory abdominal ostia, but the fact that the former never unite with the main funnel area or Müllerian duct, but end blindly. From these accessory tubes, with their supporting mesoderm, which may be grooved out from the main tubal mesentery and remain connected with it only by a narrow stalk, the occasional "hydatid of Morgagni" is thought to arise.

The completed Müllerian duct now possesses a large lumen relatively as well as absolutely larger than in previous specimens, lined by high columnar epithelium and lies just subjacent to the covering epithelium of the Wolffian ridge. The Wolffian duct lies medial and dorsal, the two being contained in a portion of the Genital ridge.

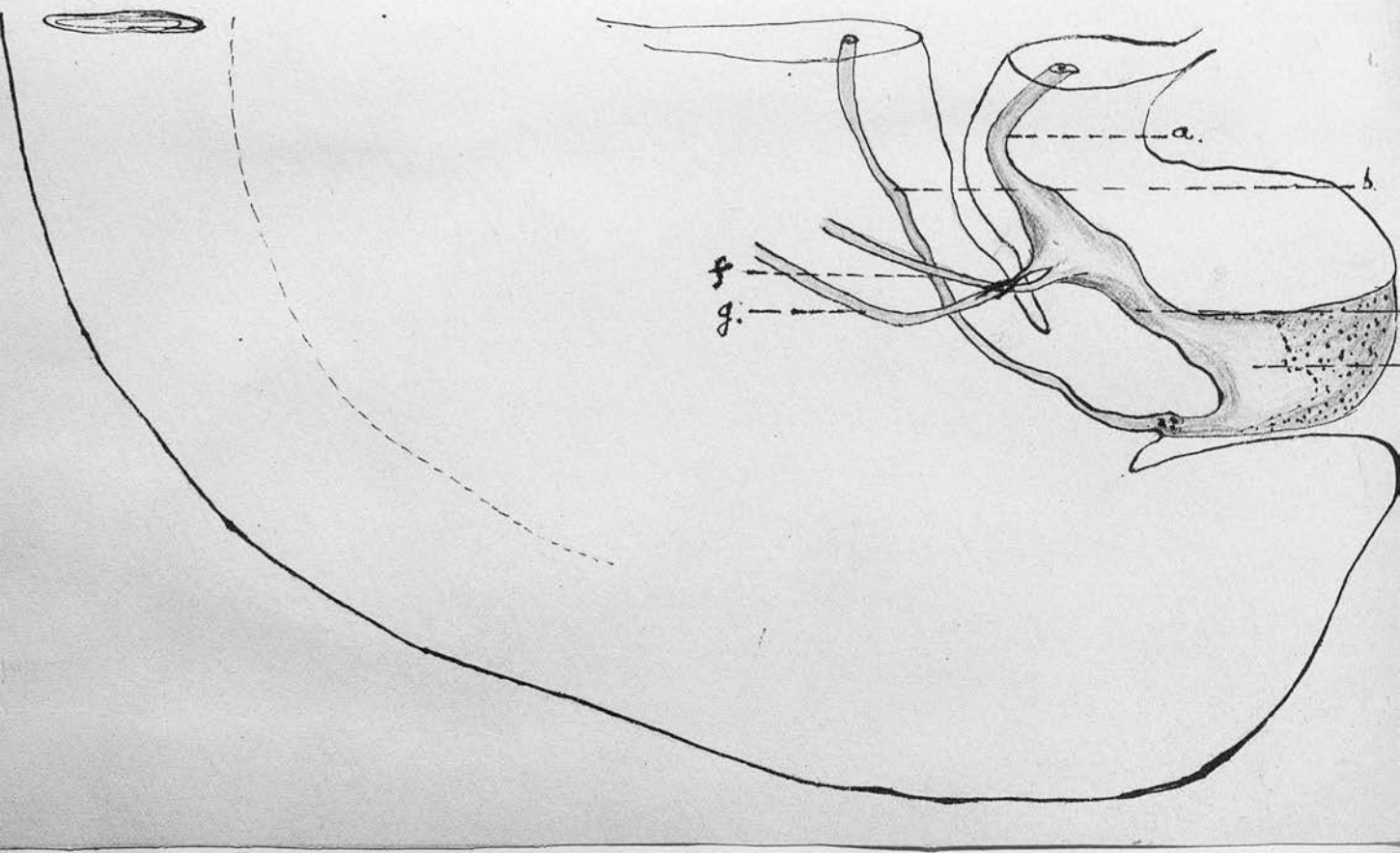


Fig. 10. 15 mm. embryo x 50. Sinus etc. (a) = allantois (b) = rectum
 (c) and (d) = pars pelvina and pars phallica of sinus. (f) = Wolffia
 duct (g) = ureter.

As yet the Müllerian and Wolffian tubes are both contained in a common mesodermic fold - the tubar mesentery.

The Müllerian duct terminates on the right opposite the 11th T.V. and on the left, opposite the disc between the 10th and 11th T.V. by becoming solid and flattened out on the anterior aspect of the Wolffian duct, where it is gradually lost sight of. (See Figs. 7 and 8.) I can distinguish no true histological connection of any kind between the two ducts.

Sinus 15 mm. (See Fig. 10.) The separation of the ventral cloaca into urethro-vesical anlage, pars pelvina and pars phallica of the urogenital sinus is better marked but the rectum does not yet possess an absolutely separate opening on the skin surface. The funnel-shaped depression on the postero-lateral wall of the future bladder has practically disappeared, but the ureter and primary excretory duct still enter a common orifice.

The anterior and cephalic part of the pars phallica of the sinus is here filled by up cells ? remains of cloacal membrane. The lateral sinus walls are smooth.

Sinus 16 mm. (See Fig. 11.) Certain changes are well marked in this specimen. The genital tubercle is prominent and the division of the cloaca into anterior and posterior parts is now complete. The rectum, therefore possesses an opening on to the skin surface, independent of, and completely separated from, that of the ventral cloaca.

The division of the ventral cloaca into its constituent parts is now plainly seen, the upper wide part -

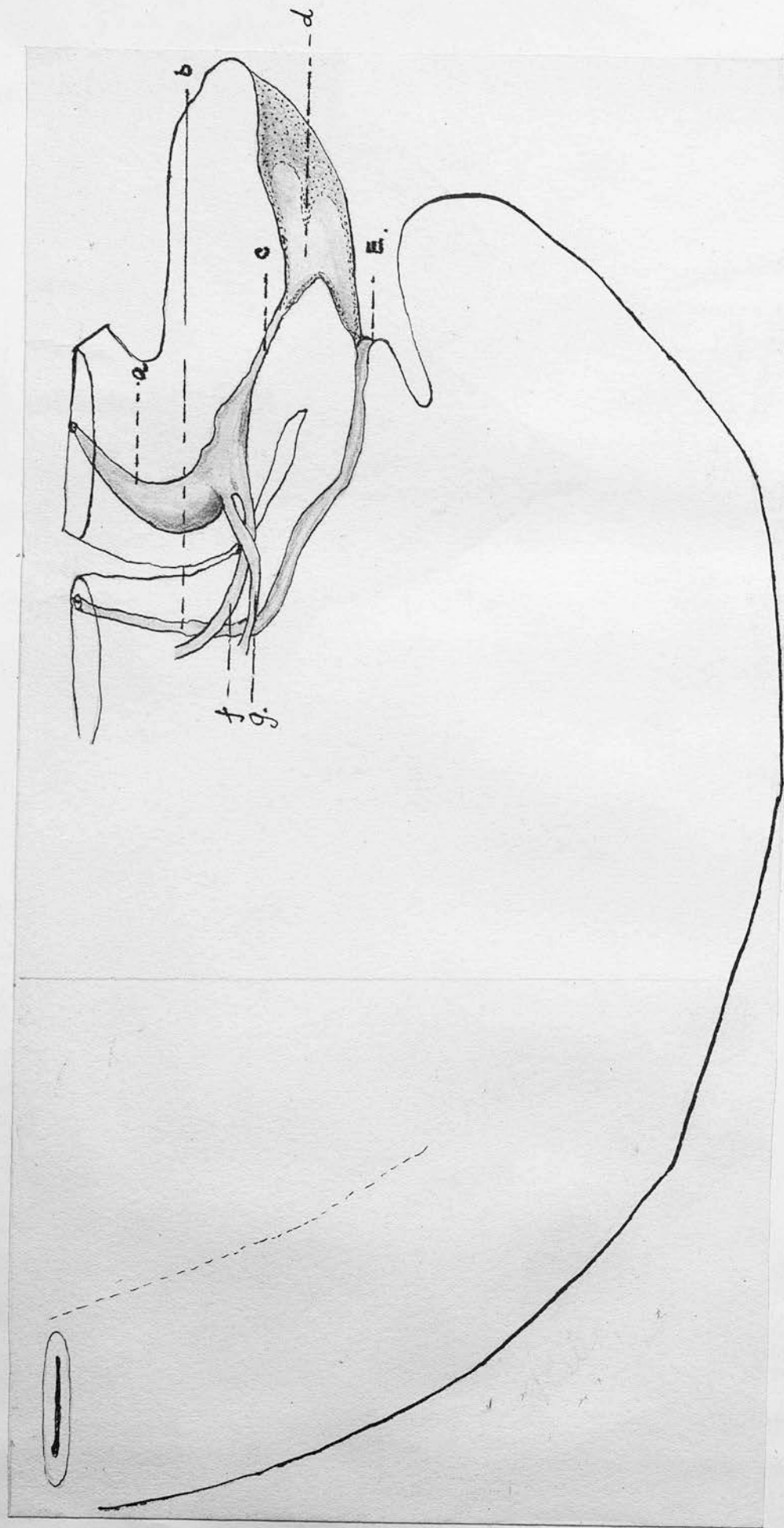


Fig. 11. 16 mm. embryo x 50. Sinus etc. (a) = allantois (b) = rectum (c) and (d) = pars pelvina and pars phallica of sinus (e) = sinus (f) = Wolffian duct (g) = ureter.

urethro-vesical anlage, the middle narrow portion = pars pelvina and the lower wide portion = pars phallica of the urogenital sinus, by which names the various portions of the ventral cloaca will now be known.

There is little trace of the former deep funnel-shaped depression in the bladder wall, and the ureter and primary excretory ducts now have independent orifices, which, however, lie in contact side by side.

The epithelial "filling in" persists in the roof and towards the anterior or ventral part of the pars phallica of the sinus - lateral sinus wall smooth.

18 mm. Embryo. The duct here commences about the level of the 10th and 11th thoracic segment as a cellular thickening and depression on the outer side of the Wolffian ridge. This area is here rather extensive, spreading over the outer half of the anterior, and the larger part of the external surface of the tubar portion of the ridge, into the substance of which it is almost at once depressed at one main and several subsidiary sites. (See Figs. 12 & 13.)

The main depression forms a deep funnel-shaped cleft, directed from the outer aspect of the ridge, internally, and possesses well marked dorsal and ventral lips by fusion of which a rather oval-lumened tube, lined by high columnar epithelium, is formed. The lesser depressions develop lumina which join the main duct after its completion and form extra abdominal ostia - fimbrial anlagen - 2-3 of which lie dorsal to the main tubal ostium, and one, at least, very deep and well marked with epithelial covered lips, ventral to the main opening; this

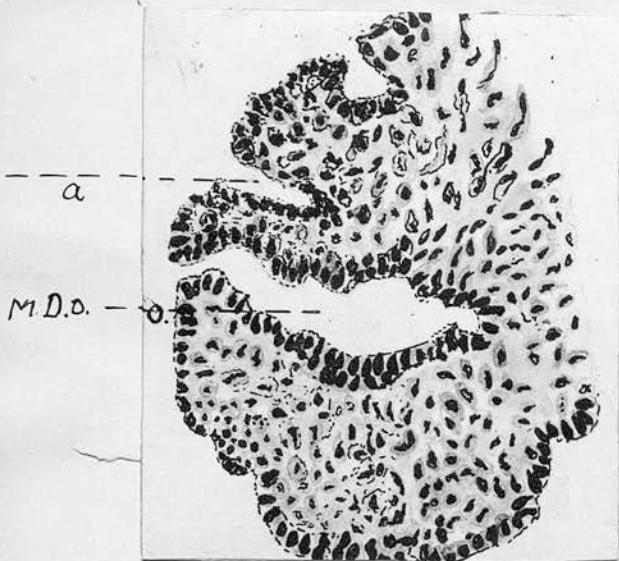


FIG. 12.

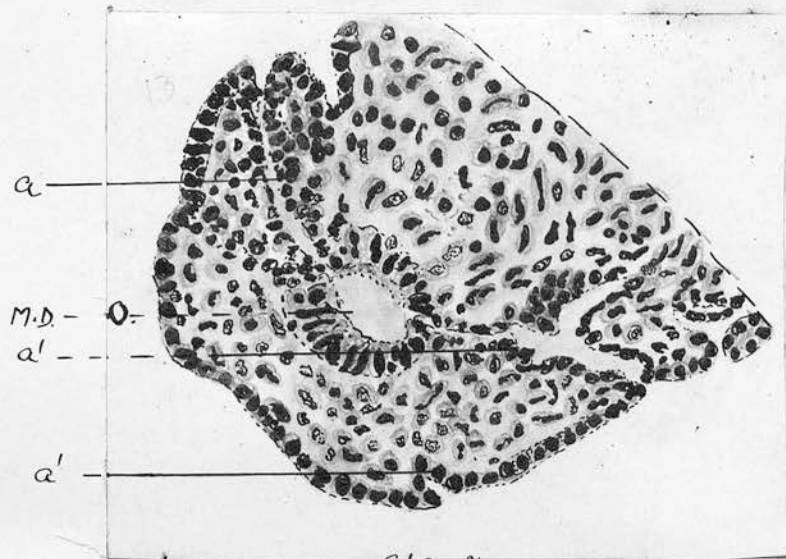


FIG. 13.

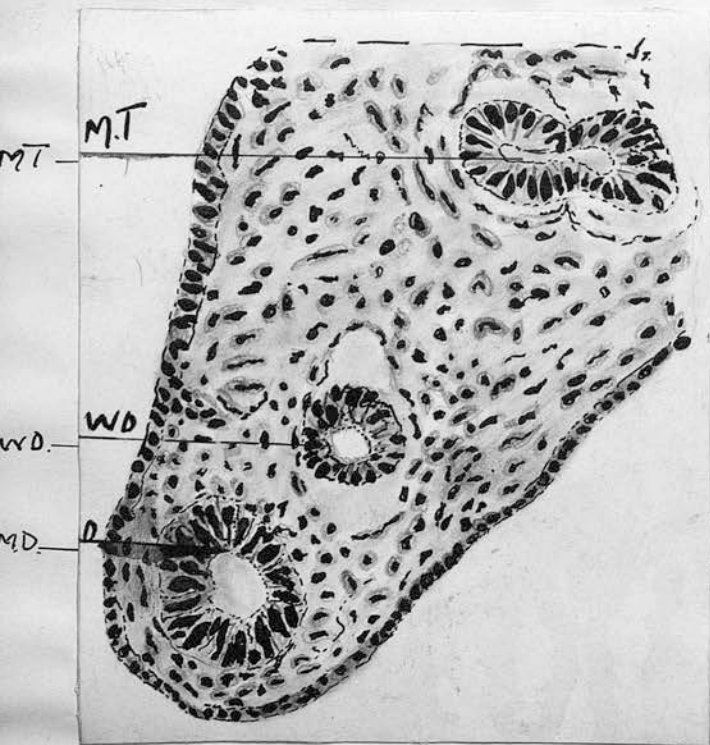


FIG. 14.

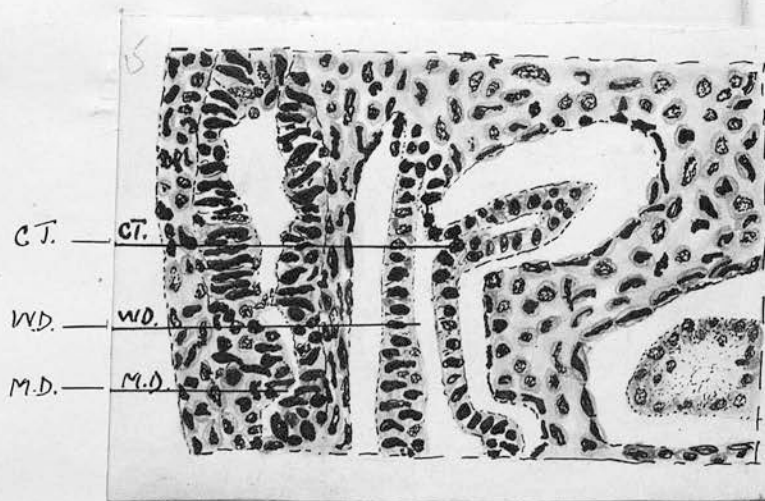


FIG. 15.

Figs. 12, 13, 14 and 15. 18 mm. embryo x 32P 12 & 13 show abdominal ostium of Müllerian duct = M.d.o. with accessory ostia (a) (a¹) 14 shows relation of Müllerian duct (M.D.) to Wolffian duct (W.D.) and Mesonephric tubule (M.T.) 15 shows termination of Mullerian Duct (M.D.) near Wolffian duct (W.D.) here receiving a collecting tubule (C.T.)

is possibly an early rudiment of the fimbria ovarica.

Followed caudally, the Müllerian duct lies in a specialised portion of the genital ridge - tubar mesentery, as previously described. In this specimen, by small dorso-lateral and ventro-lateral indentations, the portion of the mesentery carrying the Müllerian duct is becoming sharply marked off. (See Fig. 14.)

The Müllerian duct, has by this stage, extended much further caudally, and an upper vertical, intermediate horizontal, and the beginnings of a lower vertical part can be distinguished. The duct ends by becoming reduced to a solid cone of cells some distance from the mid-line. (See Fig. 15.) The terminal solid cone is not in contact with the Wolffian duct, and lies at the level of the disc between the first and second lumbar vertebrae. I can detect no mitotic figures, i.e., signs of very active cell division, in this terminal solid portion.

The Müllerian duct - after surface contact at the epithelial funnel area is lost and the tube completed - extends caudally partly by interstitial increase in length of the whole structure but also by special growth at the solid, conical tip, into which the duct can be traced.

This solid terminal portion has been described as having a bulbous outline - and exhibiting all the characteristics of a cone of growth, i.e., mitotic figures etc., but I have not been able to verify these statements in my specimens.

It has been noted that in my 18mm specimens the solid terminal portion of the Müllerian duct lies between the

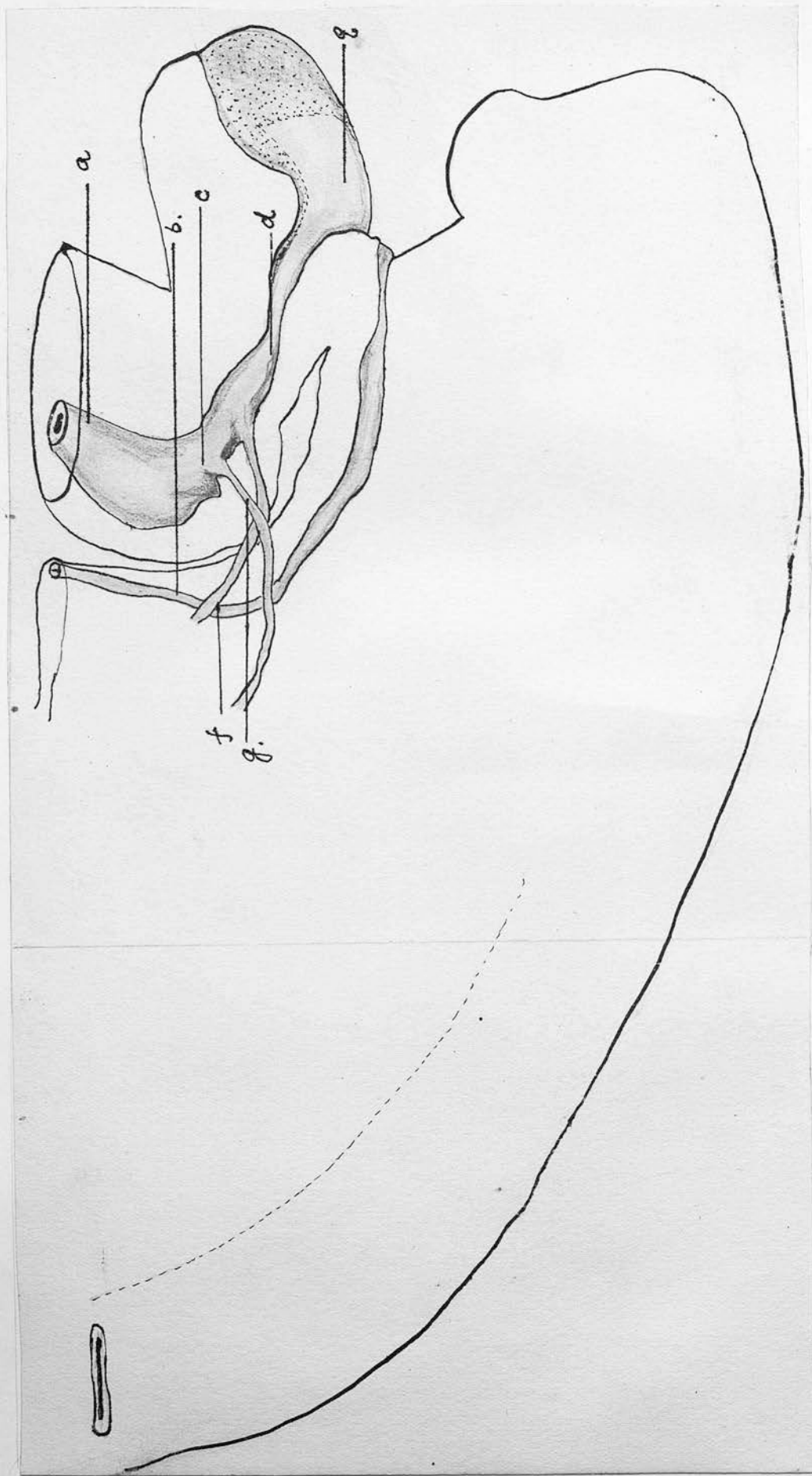


Fig. 16. 18 mm. embryo x 50 sinus etc. (a) = allantois (b) = rectum (c) = vesical anlage (d), (e) pars pelvina and pars phallica of sinus (f) = Wolffian duct (g) = ureter.

Wolffian tube and the coelomic epithelium covering the tubar mesentery, but not in contact with either at any time during its course. Growth caudally therefore takes place quite independently of any traction from or communication with, either of these two structures. The lumen of the tube in loco, forms *pari passu* with the outgrowth of the cone, and is frequently discontinuous.

Sinus 18 mm. (See Fig. 16.) shows little important change from the immediately preceeding specimen. An area of bladder wall, however, now intervenes between the openings of the ureter and primary excretory ducts which are thereby rendered quite independent.

The epithelial filling in of the anterior and upper part of the phallic sinus is still present. The lateral sinus wall has here a somewhat wavy or undulating surface, possibly due to a fault of fixation and preparation, but no grooves are present which penetrate into or produce impressions on the enclosing mesoderm.

28 mm. Embryo. The tube here begins at the level of the 11th and 12th thoracic segment, but the funnel area cannot now be definitely distinguished. The Müllerian duct appears to arise from an aggregation of small depressions, situated in the epithelium covering the outer aspect of the genital ridge. The site of the main indentation, corresponding to the funnel area in earlier specimens, lies on the outer aspect of the genital ridge, has an epithelial thickening at its base, and, by approximation and union of its ventral and dorsal lips, forms the abdominal ostium

of the Müllerian duct.

The Wolffian or tubar mesentery is early and well defined, and a partially isolated mesentery carrying Müllerian duct only, is marked off by dorsal and ventral indentations from its external aspect. The Müllerian duct runs caudally external to the Wolffian duct, which separates it from the mesonephros. It now possesses an upper vertical portion, an intermediate horizontal portion which approaches the peritoneum covering the lateral pelvic coelmic wall and then runs ventral to the floor of the coelomic cavity, and a lower vertical portion.

The intermediate horizontal portion gradually changes its relation to the Wolffian duct passing over it from its external aspect, to lie on its medial side. This change of position is rather due to a shifting of surrounding relations than a true crossing, and is produced by a rotation, on its long axis, of the genital ridge whereby the antero-external aspect swings somewhat medially and caudally while the postero-medial aspect swings correspondingly laterally and cephalically with a consequent change in the relation of the contained ducts. Thus the Müllerian duct changes its lateral position in the ridge to one at first ventral and then medial to that of the Wolffian duct, in the genital cord.

In the terminal part of their intermediate horizontal portions the Müllerian ducts lie just beneath the epithelium of the ventral wall of the coelom and between this and the Wolffian ducts. Just external to the mid-line, the four ducts turn ventrally (and caudally) at a well

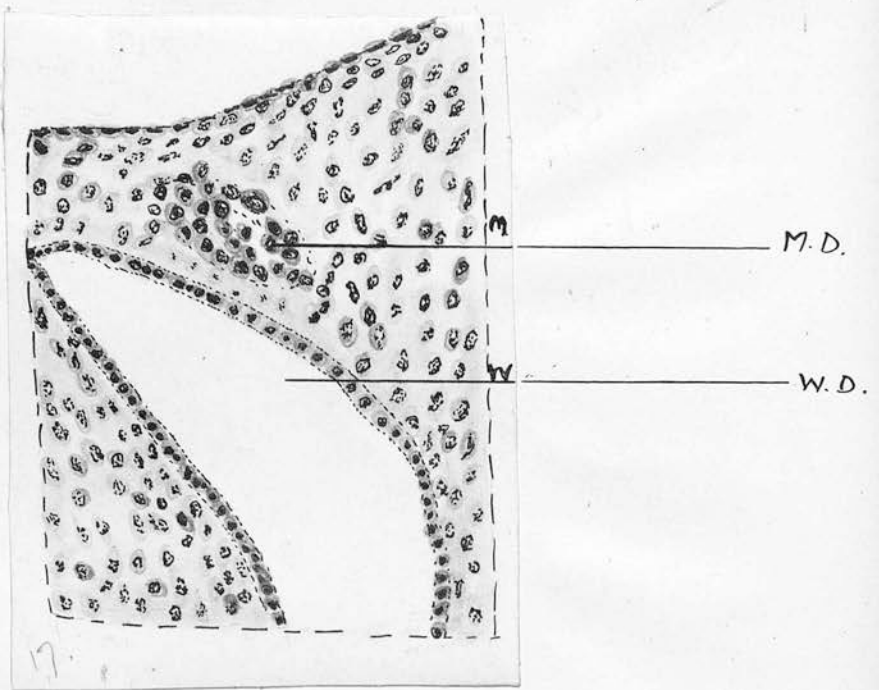


Fig. 17. 28 mm. embryo x 320. Termination of Müllerian duct (M.D.) near internal to Wolffian duct (W.D.)

marked angle, to enter the lower vertical portion of their course. The Müllerian ducts now shortly terminate by becoming solid (at about the level of lumbar vertebra 1-2) without contact with each other or with their corresponding Wolffian duct (See Fig. 17.) The latter absence of contact is possibly due to shrinkage of the specimen.

The mesoderm surrounding the terminal vertical portions of the four ducts, forms the anlage of the future genital stalk but neither it, nor the mesoderm surrounding the Müllerian tube shows as yet any sign of condensation or differentiation.

Sinus 28 mm. The orifices of ureter and primary excretory duct are now separated by a wide area of bladder wall, whilst the Müllerian duct has reached a much more caudal level than in former specimens and now terminates in contact with the primary excretory duct - henceforth to be known as Wolffian - a short distance above and posterior to the sinus.

As remarked above, there has been a very definite growth of that portion of the bladder wall intervening between the uterine and the Wolffian orifices.

The cranial portion of the urogenital sinus forms the future urinary bladder of which the portion intervening between the ureteric and Wolffian openings forms the trigone.

The sinus here possesses a low keel-like longitudinal crest on its posterior wall = posterior urogenital crest, on either side of which a groove is present.

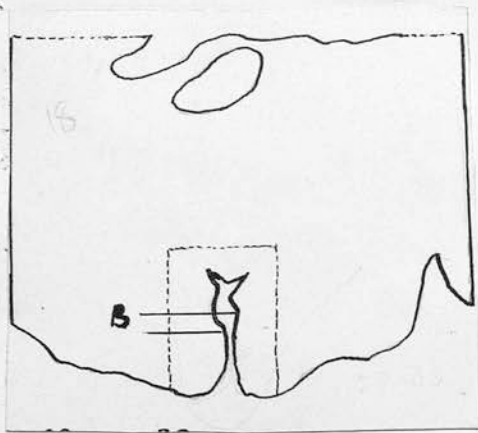


FIG. 18.

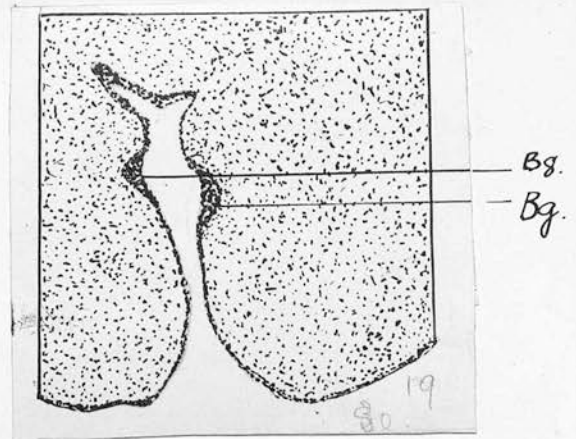


FIG. 19.

Figs. 18 and 19. 28 mm. embryo (18) x 30, (19) x 80 to show first anlage of Bartholin's groove (B) and Bartholin's gland (Bg)

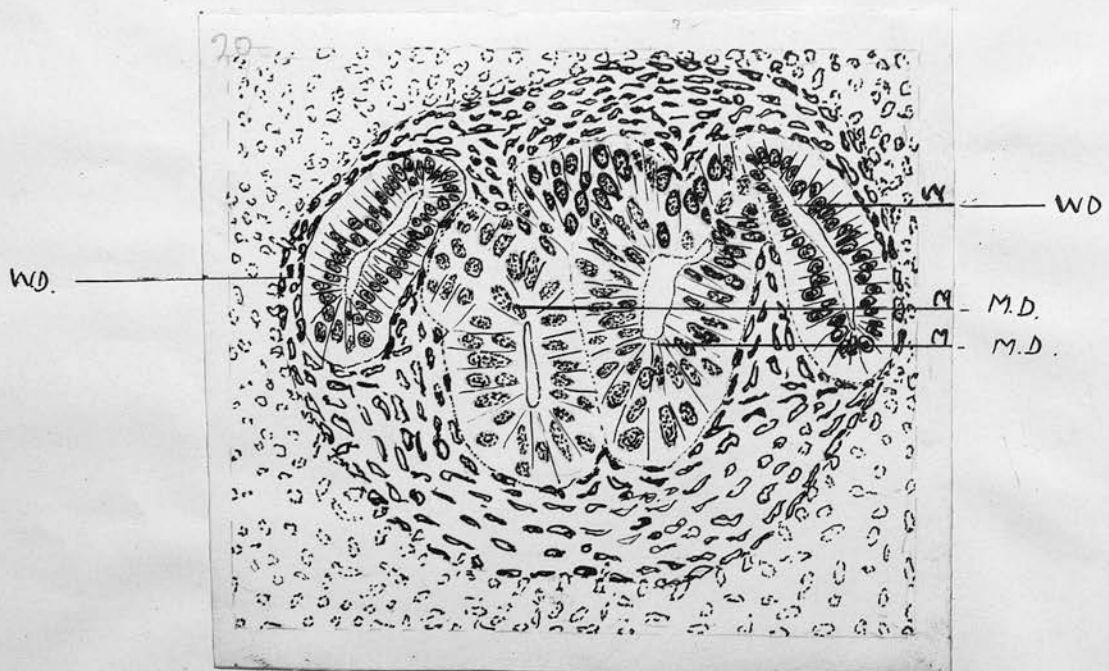


Fig. 20. 30 mm. embryo x 320. Commencing union between Müllerian ducts (M.D.) and Wolffian ducts (W.D.).

On the lateral sinus wall, lying about the junction of its posterior third with its anterior two thirds, is a well marked longitudinal groove in the base of which the presence of epithelial proliferation or budding can be distinctly seen. This forms the first anlage of Bartholin's groove and gland. (See Figs. 18 and 19.)

30 mm. Embryo. Note. In this specimen, the sections are somewhat thick and torn in places and description of histological detail is therefore difficult.

There is little of interest to be noted in the upper vertical and intermediate horizontal portions of the Müllerian Tube.

The terminal or lower vertical portions of the Müllerian ducts lie between the two Wolffian ducts. The mesoderm surrounding the four ducts is now somewhat condensed. This is the early genital stalk.

Union between the two Müllerian ducts can be first made out in this specimen - details being as follows. As the two Müllerian ducts run caudally between the Wolffian ducts in the genital stalk they approximate to each other, their medial walls come into contact, and the two ducts become surrounded by a common capsule of mesoderm. (See Fig. 20.) Between the tall columnar cells lining the approximated Müllerian ducts, are smaller, oval or round, nucleated cells forming the condensation around the Müllerian ducts. The capsular cells possibly arise from these smaller units.

This terminal or "Bud" portion of the Müllerian ducts lies on the dorsal wall of the urogenital sinus, that portion of the mesoderm which carries the bud projecting a little into the sinus, and having the sinusal openings of the Wolffian ducts on each side. This rounded projection on which the Müllerian ducts terminate at this stage is known as Müller's Tubercle.

As the two Müllerian ducts lie with their inner walls in contact, these latter break down, at first posteriorly, with the formation of a horse-shoe-shaped common cavity, which gradually becomes a transversely-placed slit-like one. This, through approximation of its anterior and posterior walls (and possibly from multiplication of its lining cells), becomes reduced to a solid epithelial bud which again at a lower level has a somewhat double appearance, showing that the union of the two Müllerian ducts takes place most completely in the middle third of their contact area. This Müllerian union, with its surrounding condensation, takes place on the dorsal aspect of the urogenital sinus, the posterior wall of which is thereby projected into its cavity to form the low prominence of Müller's tubercle. On either side of this, lie the sinusal openings of the Wolffian ducts, and, while the prominence is covered by the epithelium of the sinus and contains the Müllerian bud, these two epithelia are not in contact at any point.

The Müllerian duct extends to the level of the 4th lumbar vertebra in this specimen.

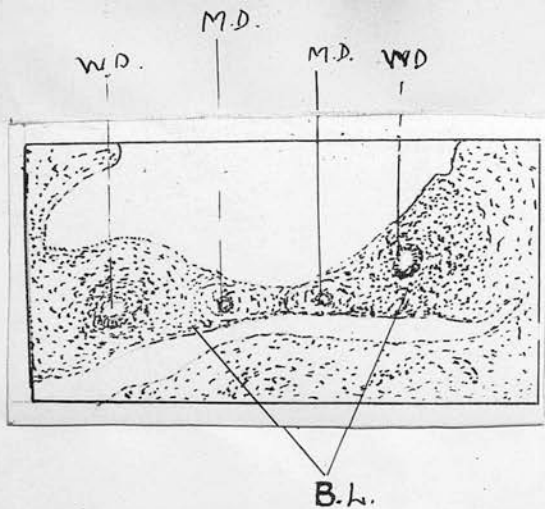


FIG. 21.

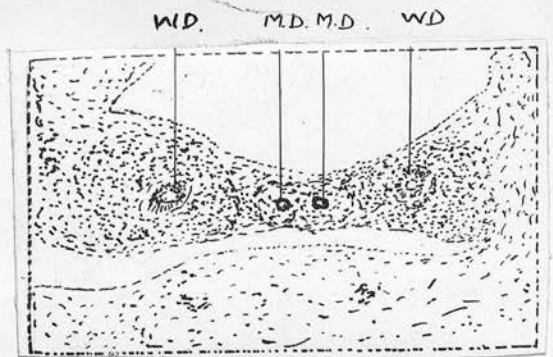


FIG. 22.

Figs. 21, 22, and 23. 38 mm. embryo x 50. To show junctions of Müllerian ducts (M.D.) and formation of Broad ligament (B.L.) (W.D.) = Wolffian duct.

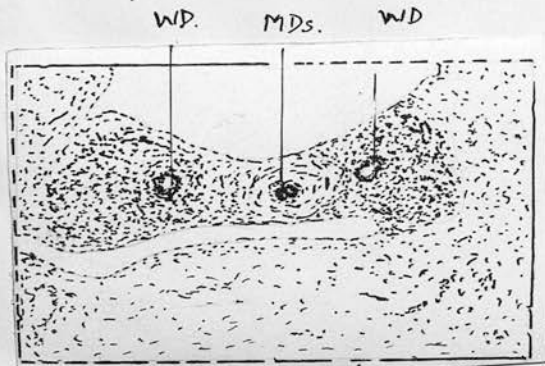


FIG. 23.

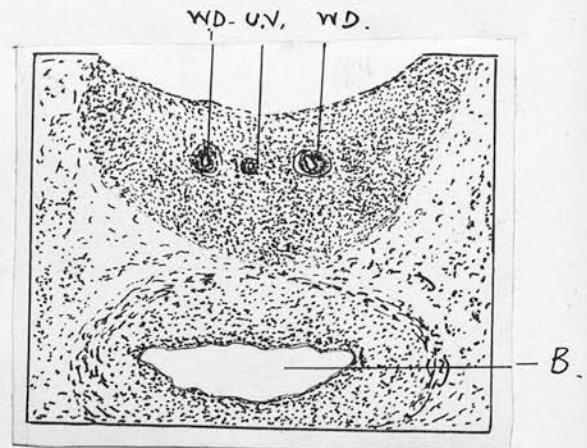


Fig. 24. 38 mm. embryo x 50. Utero-vaginal canal (uv.) surrounded by dermic condensation, (W.D.) = Wolffian duct (B) = bladder.

38 mm. Embryo. The commencement of the Müllerian duct is unfortunately not included in this block. When first met with, the tube is a well formed, epithelial lined duct, lying in the specialised outer division of the genital mesentery, the tubar mesentery. The Wolffian duct lies internal to it between it and the degenerating mesonephros, but is not included in the tubar mesentery.

While the mesoderm surrounding the tube is only slightly condensed, its cells are concentrically arranged round it. On careful examination with the high power, these concentrically arranged cells appear to be derived from the small cells filling in the interstices of the columnar lining of the tube. No mitoses can, however, be observed, and therefore the point cannot be considered to be conclusively proved.

Carried in its mesentery, the tube runs at first caudally, with the Wolffian duct and its tubules lying medially. Then, as rotation occurs, the Wolffian duct passes posteriorly and comes to lie postero-lateral to the Müllerian. Having reached the lower or caudal part of the lateral wall of the coelomic cavity, i.e., the lateral pelvic wall, the genital mesentery with its specialised tubar portion projects as a transverse fold into this cavity, carrying with it its enclosed ducts, so that these, from their former vertical direction, now run horizontally across the pelvic cavity, as a low ridge, lying just posterior to the bladder. This transverse septum, so formed, is the anlage of the broad ligament, and, as will be described later, is in relation with the early

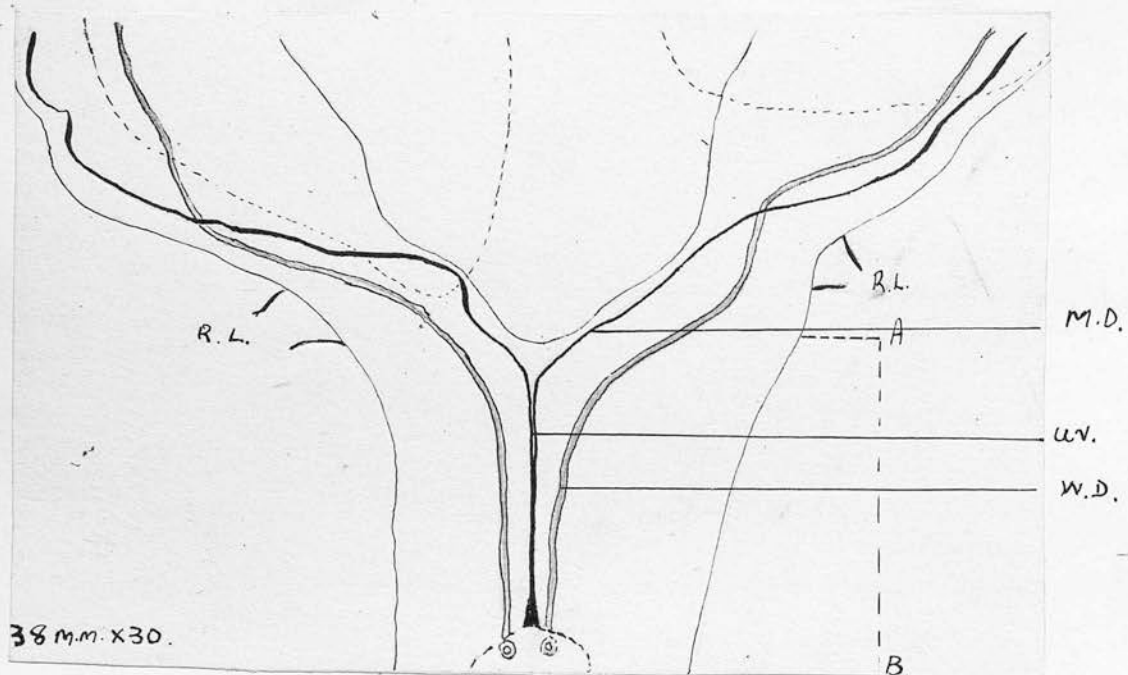


FIG. 25.

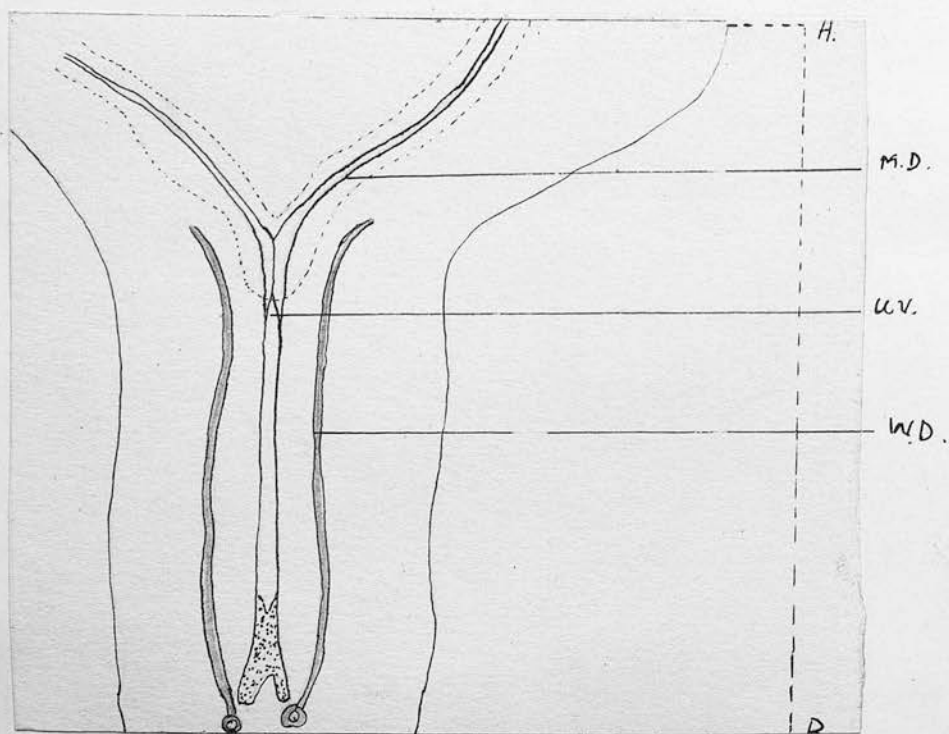


FIG. 26.

Figs. 25 and 26. 38 mm embryo (25) x 30, (26) x 50 Linear reconstruction seen from the front (25) to show incomplete fusion of Müllerian ducts (M.D.) in proximal and distal points of utero-vaginal canal (uv.) (W.D. = Wolffian duct).

anlagen of the Round and Ovarian ligaments.

The two Müllerian ducts, lying in their respective lateral halves of the Broad Ligament, approach the mid-line, each being surrounded by a fine, but quite definite layer of circularly arranged cells. Union takes place by fusion of their medial walls, the circular fibres surrounding the individual ducts, being replaced by concentric "fibres" which are common to both the fused but as yet ununited ducts. Again these later common circular fibres persist only until fusion of the two Müllerian ducts to form one common utero-vaginal canal - which is brought about by disappearance of the common medial wall - has taken place. (See Figs. 21, 22, 23.)

With fusion of the Müllerian ducts the direction of their course is altered and from running horizontally they now run in a vertical direction caudally - lower vertical portion. (See Figs. 24 and 25.)

The Wolffian ducts lie on either side of the common utero-vaginal canal, but not in contact with it, the three tubes being contained in a slightly condensed area of mesoderm, distinct from that surrounding the bladder, which is anterior. (See Fig. 26.)

As the utero-vaginal canal (the lower vertical portion) is followed caudally, its lumen becomes filled by epithelial cells which are derived by multiplication of the cells lining its cavity. At the same time the canal again assumes a double character which persists until its termination at the Müllerian tubercle. The

Fig. 27. 38 mm. embryo x 70.
Fusion of Müllerian
ducts (M.D) on Mül-
lers Tubercle (M.T)
(W.D.) = Wolffian duct
(S) = Sinus.

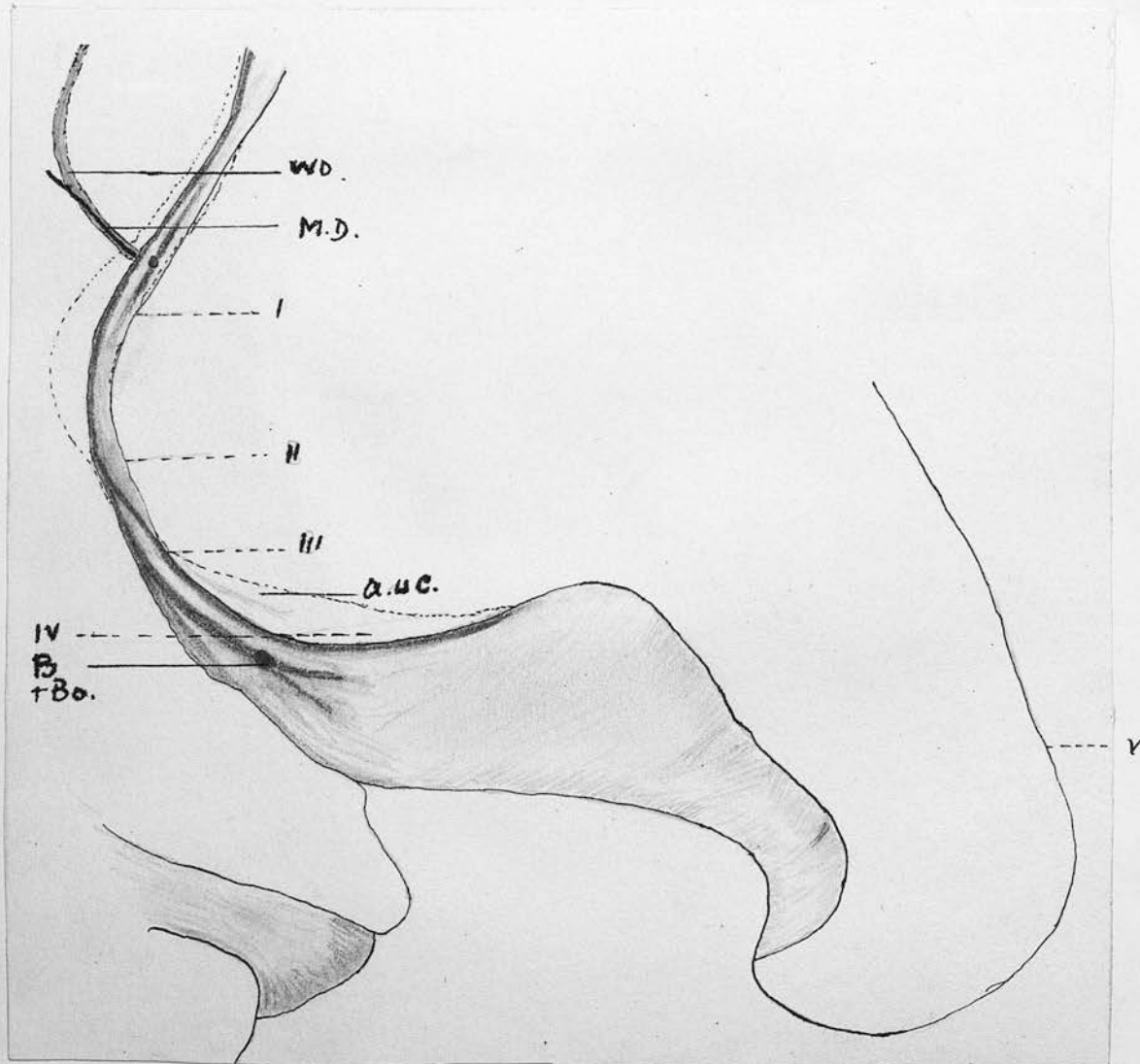
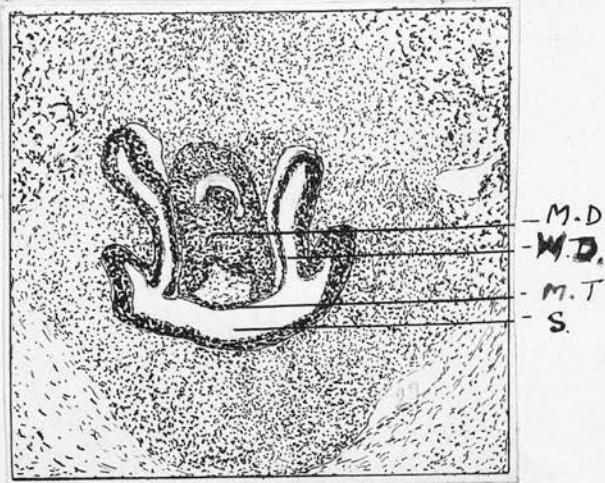


FIG. 28.

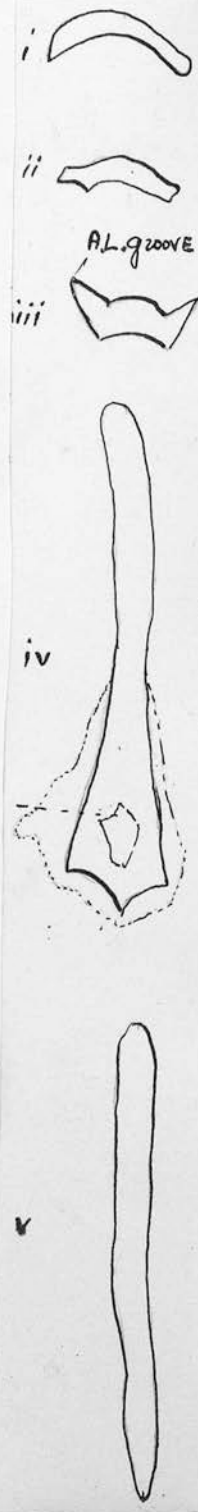


FIG. 29.

Figs. 28 and 29. 38 mm. embryo x 70 (28) seen from the side (29) Transverse sections at levels, i, ii, iii, iv, v, in Fig. 28 (W.D.) = Wolffian duct (M.D.) = Mullerian duct (a.u.c.) = anterior urogenital crest (B) = Bartholin's groove and (B.o.) orifice of Bartholin's duct.

utero-vaginal canal here terminates as a common, but more or less double solid utero-vaginal epithelial bud, on the Müllerian tubercle in contact, but not blending with the sinus epithelium covering this latter.

The Wolffian ducts open into the sinus as patent tubes on either side of the Müllerian tubercle, having no connection with its contained epithelial Müllerian or utero-vaginal bulb. (See Fig. 27.)

It can be seen from this specimen that the union of the Müllerian ducts is still incomplete, it being best marked in the middle $\frac{1}{3}$ of their lower vertical portion, where a common cavity is formed, but less complete above and below this level, where the double character of the Müllerian canal is still very evident.

Sinus 38 mm. (See Figs. 28 and 29.) The vesico-urethral anlage shows a well marked differentiation into an upper wider portion (bladder) and a lower narrower portion (urethra). The united Müllerian ducts reach the posterior wall of the urogenital sinus as a solid epithelial bud, in contact, but not blending with the cells lining the sinus and covering the ventral surface of the Müllerian tubercle. This latter prominence is well marked here and is continued down the posterior sinus wall as a rounded longitudinal crest. (See Fig. 29. - i, ii, iii,) There is at first no anterior urogenital crest, but a broad shallow longitudinal groove which, more caudally, becomes narrowed by the development of two small longitudinal crests - the relief of the inner wall of this part of the sinus now

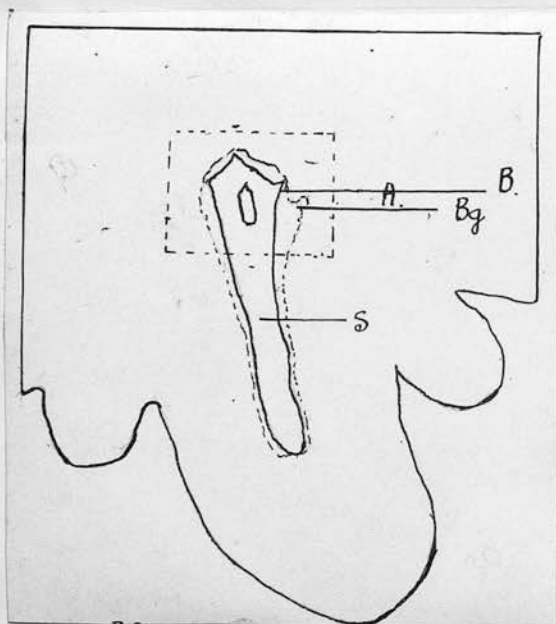


FIG. 30.

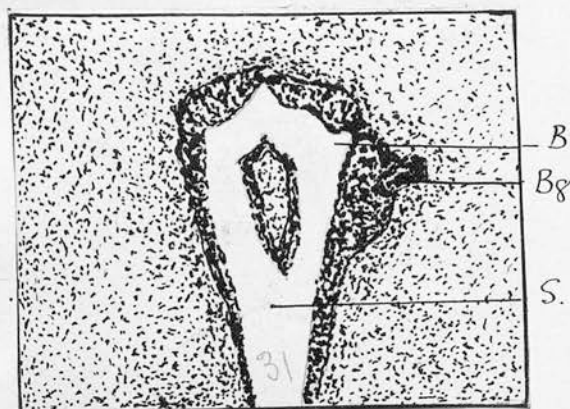


FIG. 31.

Figs. 30 and 31. 38 mm. embryo (30) x 30, 31 x 80 to show Bartholin's groove (B) and anlage of Bartholin's gland = (Bg.) (S) = Sinus.

showing posteriorly a longitudinal crest + 2 small laterally lying longitudinal grooves, while corresponding to this, on the anterior wall is a longitudinal groove bordered laterally by two small longitudinal crests (See Fig. 29, level iii.) At the junction of the anterior and posterior walls there is a deep groove or recess directed antero-laterally and becoming more anterior. It is by means of these antero-lateral grooves that communication is first brought about between the pelvic and phallic portions of the sinus, the intervening anterior wall being retained as a single prominent anterior urogenital crest.

The two longitudinal grooves on the posterior sinus wall are continued into the phallic portion and, each becoming more lateral, send out an epithelial bud into the surrounding mesoderm. This epithelial bud forms a definite small solid acinus - the first anlage of Bartholin's gland (See Fig. 29 level iv. and Figs. 30 and 31).

The pars pelvina of the sinus, in this specimen, is still very long and narrow in proportion to the shorter and wider pars phallica. The walls of the external and ventral part of the pars phallica are smooth, the earliest formed groove being that from the epithelium lining of which Bartholin's gland and duct are formed.

Note. This is the earliest specimen in which I have been able to detect the primordium of Bartholin's gland (It will be remembered that Bartholin's groove was present by the 28 mm. stage). A detailed description of the stages of development of Bartholin's gland and duct will be given later in the paper. The site of the orifice or Bartholin's duct into this groove being a fixed point, is of great importance in the consideration of the meaning and extent of

the changes in relations of the various constituent parts of the sinus to one another.

The Development of the Müllerian Duct.

The development of the Müllerian duct so far as we have gone, may now be recapitulated, and the views of other writers considered.

The Müllerian duct arises from an invagination of the coelomic epithelium covering the outer surface of the Wolffian and genital area. As early as the 10 mm stage the epithelium covering this area is differentiated by becoming tall and columnar; while by the 12 mm stage this area, now to be known as the funnel area, is depressed into the interior of the ridge, so that the depression comes to possess a ventral and a dorsal lip, which by fusion enclose a rounded lumen = lumen of the Müllerian duct. These ventral and dorsal lips of the funnel area, forming the ostium abdominale tubae, do not become very well marked till the 12 - 15mm stage, where it can be seen that the ventral lip is prominent and hook-shaped, and by its outgrowth fuses with the less prominent dorsal lip. About this stage, subsidiary depressions or solid epithelial cords are seen growing into the surface of the genital mesentery, from the "funnel area". Some of these join the newly formed Müllerian duct and form extra-abdominal ostia, which are the anlagen of the future tubal fimbriae.

The Method of Formation of the Müllerian Duct.

Views of other Workers.

A. Historical

At various periods different views have been held on the origin and mode of development of the Müllerian Duct and these have been well summarised in Amann's (2) paper where he quotes the following:-

Rathke (3) (1825) working on dogs, was the first to describe the duct which he derived as an out-growth - at first blind - from the roof of the Wolffian duct, but later developing an opening into the peritoneal cavity.

Müller (4) (1830) gave a detailed description of the duct, which bears his name. Up to this time a sharp distinction had not been drawn between Wolffian and Müllerian ducts. Müller observed that, in birds, the excretory canal of the ovary, or oviduct, was distinct from that of the Wolffian body, but that the seminal duct was derived from the Wolffian canal, a view which agrees with present day opinions. Müller believed, however, that in mammals the Müllerian duct was the excretory duct of the genital gland in both sexes.

Gegenbaur (5). (1859) By studies in comparative anatomy, Gegenbaur came to the conclusion that the Müllerian duct was derivative from the Wolffian in lower vertebrates.

Balfour (6). derive the Müllerian duct from
Semper (7) the Wolffian by budding.
Hoffmann (8).

Hoffmann (8). In the Amphibians, however, according to Hoffmann and other authors, the fore-end of the Müllerian duct is derived from the coelomic epithelium, while the hinder end is still produced by out-budding from the Wolffian duct.

In the Selachians this outbudding is in the form of a hollow canal, while in the Amphibians a solid cord is present.

Müller (4). Müller's final description of the origin of the duct, confirmed by Rathke (3), Valentin (9), Kobelt (10), Bishoff (11), was that it arose by differentiation occurring in the mesoderm surrounding the Wolffian duct, and later developed a communication with the coelomic cavity.

Dursy (12)

Waldeyer (13) Dursy considered the duct arose from the epithelium covering the Wolffian ridge, as did Waldeyer who described two longitudinal folds arising on the lateral side of the Wolffian ridge, which become approximated and fuse together at their margins in a cranio-caudal direction, leaving a narrow gutter between them, to form an epithelial-lined canal.

Bornhaupt (14) describes an epithelial "insinking" in the form of a funnel-shaped depression on the lateral surface of the Wolffian ridge. The apex of this funnel grows distally between the coelomic epithelium and the Wolffian duct, and forms the anlage of the Müllerian duct.

This description of the Müllerian duct, first given by Bornhaupt, has been confirmed by practically all subsequent observers - although there are a few divergent opinions held by workers since this period.

In his paper, Amann describes an epithelial thickening and transference from the cubical to high columnar type of cell taking place on the outer aspect of the Wolffian ridge. In this epithelial ridge are developed one or more (at the most three) little canals, epithelial-lined, which end blindly, caudally and cranially. The most dorsally placed of these comes into contact with the epithelium of the Wolffian duct which here shows clear signs of proliferation apparently distinct from the canals in some places, while cells from the Wolffian duct in other situations pass to the canaliculi. Amann found at these places in the Wolffian ducts, mitosis with axes of division at right angles to the border of the duct.

In Amann's opinion the most dorsally placed of these little canals is the first anlage of the Müllerian duct, and has its origin, therefore, in the multiple-layered coelomic epithelium on the outer side of the Wolffian ridge. As soon as its cranial end has broken through, laterally, to communicate with the coelomic epithelium, the impression is given that the Müllerian duct arises through fusion of the lips of a groove. Amann's work is principally based on observations of the sheep embryo, but from his later remarks on the subject of accessory abdominal ostia and tubes, it appears he holds a similar view of the early development of the Müllerian duct in the human species.

Wichmann (15) speaking of somewhat older fetuses 30 mm, 80mm and 110mm specimens, describes an epithelial canal which in a 110mm specimen passes from the fimbrial edge to form, on the left, junction with lateral epoöphoritic canals, and

on the right, to end blindly near a similar epoöphoritic canal, and he states in this connection that in the human early foetal life, there is not seldom an epithelial union between fimbrial edge of the abdominal ostium of the tube on one hand, and the mesonephric epoöphoritic canals on the other, the epithelial cord bringing about this junction arising from a portion of the complementary canal, formed by differentiation of the primary mesenchyme which has exceptionally maintained its primary union with the coelomic cavity.

I have seen nothing to correspond with this observation.

Time of Appearance of Anlage of Müllerian Duct.

Most authors give the time of the first appearance of the anlage of the Müllerian duct as from 8-12mm, the earliest appearance being given by His, quoted by Spuler (16), who gives the epithelial thickening leading to the commencement of the Müllerian duct as 7-7.5mm. In our specimens, the epithelial thickening, which forms the early anlage of the Müllerian duct, was first noticed at 10mm stage.

The Developmental Value of the Ostium Abdominale Tubae.

By some authors the abdominal ostium of the tube is considered to have some ontogenetic value and to arise from the lowest pronephric tubule. Where accessory abdominal ostia are present these authors e.g., Kossmann (17) quoting Holzbach (18), consider that they may arise in remnants of pronephric tubules. Against this view is the result of the examination of specimens - e.g., in our case, a 4.9mm embryo, which shows that where remnants of pronephric tubules are present these lie always internal to the Wolffian or mesonephric duct. whereas the anlage of the developing Müllerian Duct is always lateral to this.

Accessory Abdominal Ostia and Tubes.

It has been noted in the description of the 13mm. 15mm and 18mm specimens that accessory abdominal ostia are present near the main ostium abdominale of the Müllerian duct. These are for the main part epithelial-lined depressions, which join the main funnel area either just before or just after the fusion of its lips to form the closed Müllerian tubes. Solid epithelial cords are also to be seen passing from the Müllerian epithelial area to the duct. These ostia are variable in number - often 2-3-4 are present - and they may lie either external or internal to the ostium abdominale tubae,

forming the anlagen of the future fimbriae of the tube. In our own specimens we have noted a particularly well-marked one lying internal to the main opening of the tube, and which may possibly be the anlage of the future fimbria ovarica.

Much discussion has arisen over the mode of origin and significance of accessory abdominal ostia and tubes. (For method of differentiation see note from Felix) p. 12.

On the subject of accessory abdominal ostia and accessory tubes, Felix states that he has only found the latter in the female sex. He mentions the fimbria ovarica arising about the 40-45mm stage as a grooved projection, directed towards the ovary. Felix states that accessory ostia arise as solid growths of the "funnel area." These growths separate partly from the parent tissue, and the ends which have thus become free unite with the principal funnel.

Note. (In our specimen some of the accessory ostia certainly arose as epithelium depressions, these possessing a lumen from the first).

Felix adds that accessory tubes, when present, usually lie at a more distal level - the maximum number being 4 - and that of the "double tube" or "tubar appendages" described by Kossmann, he has no personal knowledge.

Kossmann (17) in his paper, describes the appearance of 7 cases in which extra abdominal ostia, and 3 cases in which accessory tubes, were present at operation, and considers their mode of production and significance. He states that in no case where an accessory tube was present could any communication be made out with the lumen of the main tube, even in serial section. Re the mode of origin of accessory ostia and tubes, Kossmann quotes Rokitansky who considers that accessory ostia are due to irregular fusion of the lips of the "funnel area" so that a communication with the coelomic cavity is left above and below the adhesion area. The former author points out that this view does not account for the presence of numerous - e.g., in his Kossmann's case (5) - accessory abdominal ostia, nor does it explain the fact of the occurrence of accessory ostia and accessory tubes in the same specimen, and considers that an explanation is probably to be sought in the presence of multiple embryonic parallel anlagen in the funnel area - one type breaking through into the main funnel to form accessory ostia, while the other, possibly developing at a slightly later date, i.e., when the apex of the main tube has penetrated deeply into the mesoderm, fail to reach it, and remain as blind accessory tubes.

Amann considers that accessory tubes arise from the small epithelial-lined parallel canals des-

cribed by him in the thickened epithelial area on the outer side of the Wolffian ridge. This view, again, does not seem to account for cases in which there are multiple accessory ostia or tubes, and one is therefore rather forced to take the view that the epithelium covering the funnel areas possesses potentialities of downward growth into the underlying mesoderm, and that therefore epithelial ingrowths can take place at more than one area simultaneously, but as these accessory ingrowths reach and fuse the main "funnel" or fail to do so - as the result of later appearance - accessory ostia or funnels are produced.

Development of Müllerian Duct.

The newly formed Müllerian duct shortly becomes solid and terminates in apposition with the Wolffian duct, no connection, however, being made out between the two. In subsequent stages extension of the Müllerian duct in a caudal direction takes place, in part, by growth from its solid epithelial tip - the so-called "cone of growth" -, and in part by the growth of the cells along its whole length. The Müllerian duct runs caudally between the Wolffian duct and the coelomic epithelium, lying at first, with the former, in an external division of the genital mesentery which is isolated by means of indentations from the external aspect of the Wolffian ridge - tubar mesentery. In its course through subsequent stages, the Müllerian duct reaches a more caudal level, but at no time shows any connection whatever with the Wolffian duct and (except at the funnel area) with the coelomic epithelium, its downgrowth and direction being independent of these factors.

Absolute unanimity has been no means arrived at between workers as to the mode of growth or extension caudally of the Müllerian duct. It will be

remembered that in Amphibians and reptiles, the Müllerian duct is definitely connected with and indeed arises from the Wolffian duct. Amann, in his paper, states that the growth caudally of the Müllerian duct takes place mainly by proliferation of its own cells, but also by derivation of cells from the Wolffian duct and coelomic epithelium. Balfour and Sedgwick (6), working on Chickens, considered that the Müllerian duct arose through invagination of the coelomic epithelium, but that it grew at the expense of the Wolffian duct.

Nagel (19), describes in an 11-13mm embryo - an "innige Verbindung" (close connection) between the epithelium of the two ducts - Müllerian and Wolffian - which does not pass on to fusion.

Spuler (16), also, denies any connection between the two ducts and remarks that the so-called "cone of growth" in the Müllerian ducts is distinctly present in cats.

Wendeler (20) gives a good description of the method of caudal extension of the Müllerian duct and one that fits in closely with my own view. He states that this growth takes place principally at the solid apex of the Müllerian duct but there is also an intermediate growth. A strong intermediate growth leads to a pushing on of the solid end, and then formation of folds and bends, as in the later development of the tube. The formation of the lumen keeps pace with the growth caudally of the solid end in the following way:- the cells next the extending lumen irregularly placed and apparently undifferentiated, assume a taller and more wedge-like shape and arrange themselves radially, their nuclei at the same time taking up a situation nearer the outwardly directed bases of the cells. With a centrifugal contraction of the cell bodies against the nuclei, a small lumen appears towards the central point of the cell group. The lumen so formed is further developed by a multiplication of the cells and a repetition of the above process.

By the 28mm stage, having in its course, by a half spiral turn, come to lie on the median side of the Wolffian duct, the Müllerian duct terminates near the middle line and its fellow, by becoming solid.

In this connection it may be noted that Nagel (19) from the earliest stages divides the Müllerian duct into two portions, a proximal lumen-bearing portion, and a distal solid portion, and with this I am in agreement, taking the early solid apex or cone of growth to repre-

sent the distal solid portion in the early stages.

It is not until the 30mm stage that union of the Müllerian ducts - not always complete - takes place on the Müllerian tubercle, and not until the 38mm stage that actual contact is formed between the epithelial bud, arising from the termination of the fused Müllerian ducts and the sinus epithelium covering Müller's tubercle.

Nagel describes fusion between the solid Müllerian bud and the sinus epithelium - with the result, that over the summit of Müller's tubercle, the two epithelia cannot be distinguished. Whether this results from true fusion or atrophy of the overlying sinus epithelium, he finds it impossible to say.

I have not found contact until the 38mm, and fusion not until a later stage still.

It will be remembered that in describing fusion of the two Müllerian ducts in the genital cord, it was remarked that this fusion was by no means complete, the utero-vaginal canal, so formed, at its distal extremity again assuming a somewhat double appearance. This characteristic persistence and proof of the double origin of the utero-vaginal canal can be detected to a lesser degree in older specimens (see e.g. 48mm embryo).

As shown from my specimens, therefore, the union of the Müllerian ducts is most complete in the middle third of their lower vertical portion and extends up and down from here.

This view, however, is by no means endorsed by all previous workers on this subject. Tourneux & Legay (21) agree that the union of the Müllerian ducts commences about the middle to lower third of the genital cord and spreads up and down from here, but quote Koelliker (22) as fixing the commencing site of fusion at the middle, Fürst (23) and Dohrn (24) at the junction of the lower and middle third of the genital cord, while Langenbacher (25), working on rabbits, describes the union as commencing at

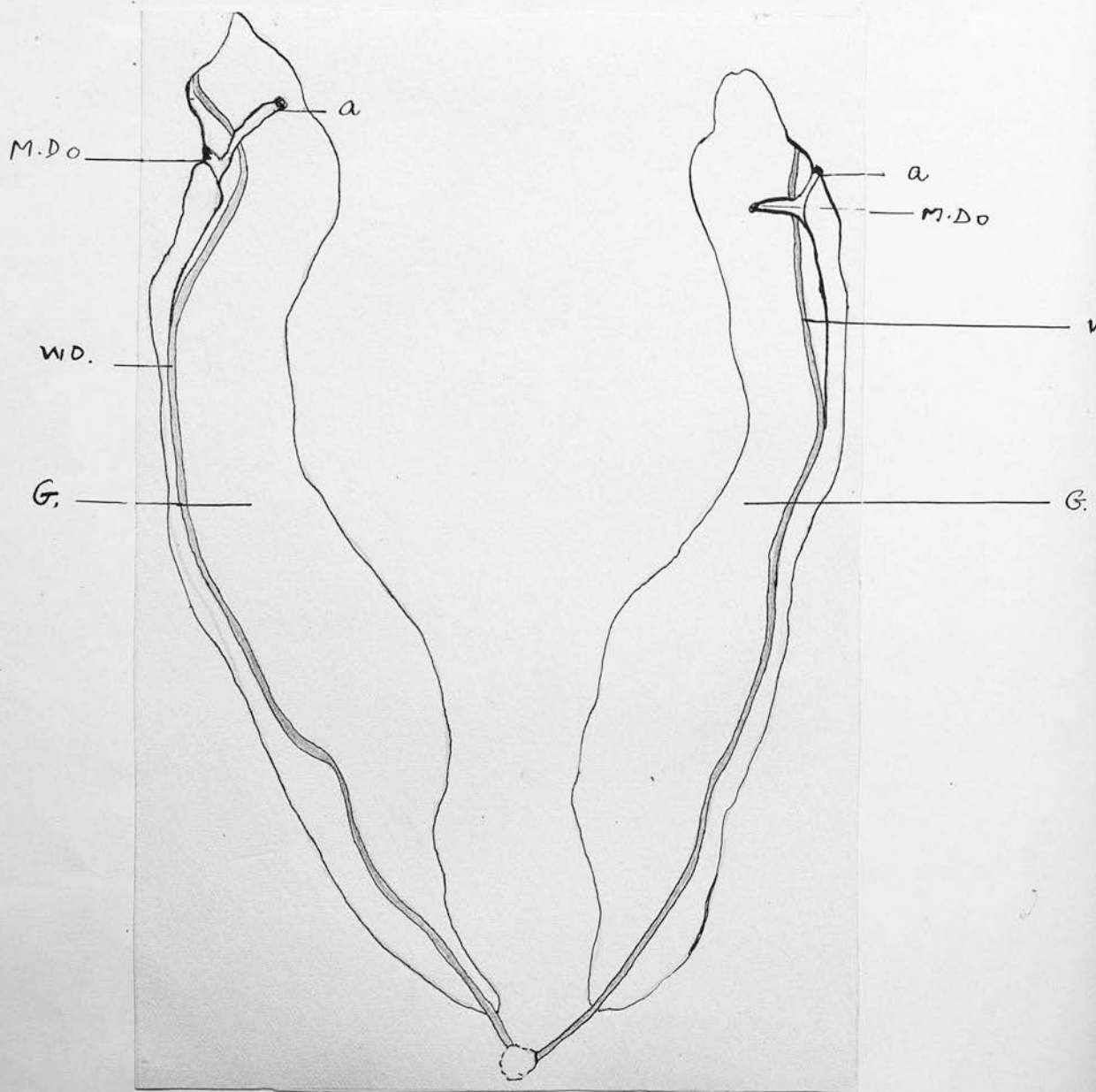


Fig. 32. 15 mm. embryo x 50. Reconstruction of Müllerian ducts (M.D.) abdominal ostium = (M.D.o.) accessory ostium, (a.O.) (W.D.) = Wolffian duct (G) = genital gland.

the vestibular extremities of the Müllerian ducts.

During the growth caudally of the Müllerian duct special attention must be drawn to:-

1. Changes in the level of the ostium abdominale tubae.
 2. Changes in the direction of growth, the duct exhibiting, as it is traced through succeeding stages, an upper vertical, a middle horizontal, and a lower vertical portion, with angles corresponding to the changes in direction of growth of these portions.
1. The changes in level of the ostium abdominale tubae may best be seen from the accompanying two tables, one made from my own specimens - these are approximate only - and the other from Felix.

<u>Table I.</u>	<u>Stage</u>	<u>Begins</u>		<u>Ends</u>
	10mm	3	Thoracic Seg:	-----
	12mm	5-6	" "	-----
	13mm	6	" "	6-7 Thoracic Seg:
	15mm	8-9	" "	11 " "
	18mm	10-11	" "	1-2 Lumbar Seg:
	28mm	11-12	" "	?2nd " "
	30mm	?		4 " "

Table II From Felix

<u>Stage</u>	<u>Begins</u>		<u>Ends</u>
12-5	7th	Thoracic Seg:	8th Thoracic Seg:
13	9th	" "	11/12 " "
14-75	10th	" "	1 Lumbar Seg:
18	10th	" "	2 " "
28-5	2	Lumbar Seg:	Müller's Tubercle
30mm.	2-3	" "	

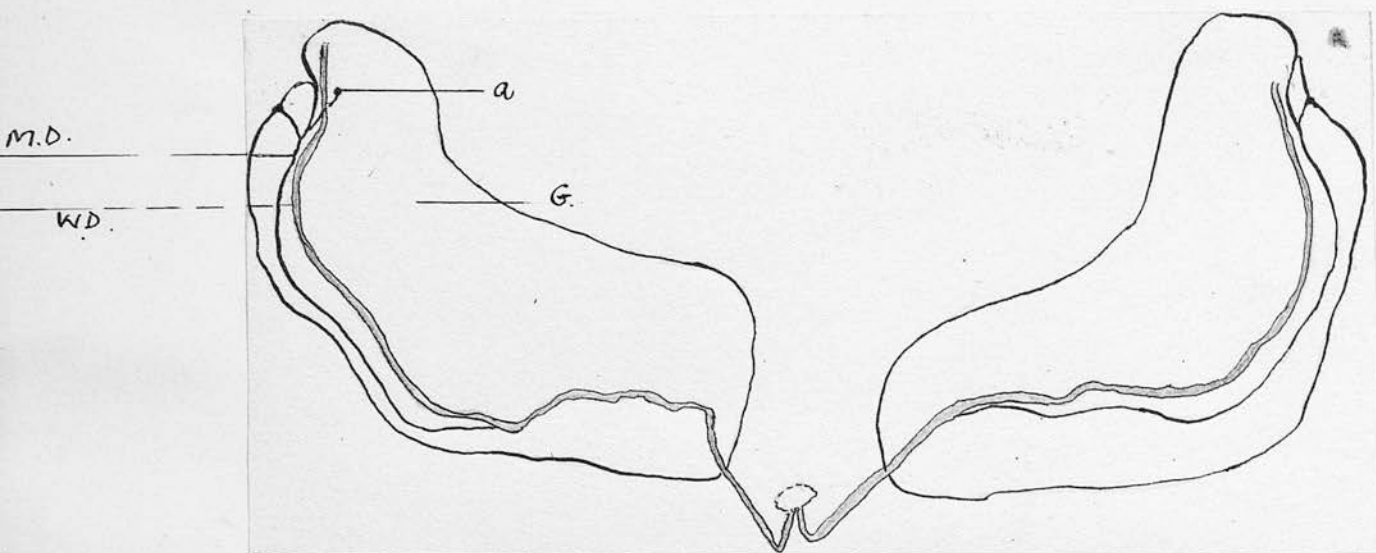


FIG. 33.

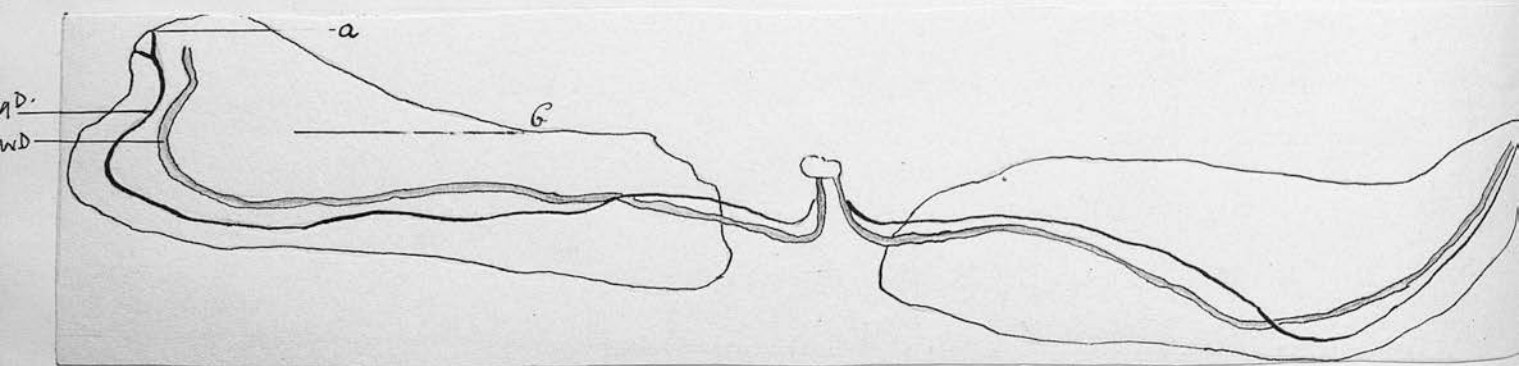


FIG. 34.

Figs. 33 and 34. (33) 18 mm. embryo (34) 28 mm. embryo x 50 (M.D.) = Müllerian duct (a) = accessory ostia (W.D.) = Wolffian duct (G) = Genital gland.

It is thus seen that the level of the abdominal ostium of the tube shifts from the 3rd Thoracic Segment in the 10mm embryo, to the 2nd Lumbar Segment in the 30mm embryo - and this with an absolute increase in the total length of the tube (e.g. from 330 μ at 12.5 mm \rightarrow 1560 μ at 19.4mm (Felix) (1D) showing that an actual change in position of the ostium abdominale tubae takes place pari passu with the growth of the tube. For comparison in length of Müllerian duct see Figs. 32, 33 and 34.

N.B. In this comparison, it is well to remember that Felix is probably employing a mode of measurement wholly different from mine, which are given in Vertex Breech lengths: hence the apparent difference.

The ostium abdominale tubae, once formed, remains constant, i.e. there is no question here, as with the Wolffian Body, of atrophy of the most cephalically lying part or tubules with-pari passu - the appearance and growth of more caudal tubules, thus allowing an apparent descent of the Wolffian Body on the posterior abdominal wall and here we must look to other factors in causing the descent. Perhaps the most important of these is the growth of the abdomen, especially in the posterior umbilical region - at a relatively greater rate than the contained Müllerian duct, which also, as it is attached to the genital ridge, is drawn down with this latter, as it descends caudally.

2. With the changes in direction of growth of the various portions of the Müllerian duct, the degeneration

of the cranial part of the urogenital fold with its principal contents has much to do, leaving as it does the upper portion of the Müllerian duct, hanging by a very loose fold, which allows curving and bending. But the true explanation of the changes in the direction of the duct's course lie rather, as we have said previously, in the development of the organs internal to the Wolffian ridge. These are the suprarenals and the metanephroi which, as they enlarge, push the urogenital folds laterally, - an increased broadening of the posterior abdominal wall allowing for this. Caudal to the metanephroi this broadening force ceases, and therefore the urogenital folds and ducts are not displaced.

This displacement above, and absence of it below, produces the bending of the ducts above described.

Further changes in the tube will be more conveniently considered when dealing subsequently with the stages in which they may arise. These stages are now about to be dealt with, and are concerned with the development of the uterovaginal canal, sinus etc.

Before passing on, however, this seems a convenient place to discuss the ultimate fate of the Müllerian ducts and at the same time to review briefly views as to the origin of uterus, vagina etc.

My opinion, in common with that of a great number of observers, is that the Müllerian ducts form ultimately the tubes, uterus, and vagina in its entirety, and the vaginal layer of the hymen.

Quoting Tourneux & Legay who themselves believed that the fusion of the Müllerian ducts gave origin to tubes, uterus and vagina (?participation of Wolffian ducts in the formation of this latter - see later) - first observers believed that the uterine cavity was formed from an excrescence of the posterior part of the urogenital sinus, which formed uterine body and vagina, the Müllerian ducts only forming Fallopian tubes, and uterine horns (Rathke 1832). J.Müller,

in 1830, expressed the view that the uterus was a formation of the Müllerian ducts, the vagina being formed from the sinus, which view was reproduced by Lilienfeld (26) in 1856. Valentin considered that the sinus formed the vagina, but by a sort of longitudinal fission, the anterior and superior division forming the urethra, while the lower and posterior part formed the vagina. All authors, indeed, up to this date, considered that the urogenital sinus participated in the formation of the lower part of the utero-vaginal canal.

Briefly, there is a concurrence of opinion that the Müllerian ducts are responsible for the formation of the Fallopian tubes, uterus, and for some part of vagina, but the extent of their participation in the formation of this last, and the exact mode of its origin is a subject over which unanimity of opinion has not yet been reached and which will receive due attention later.

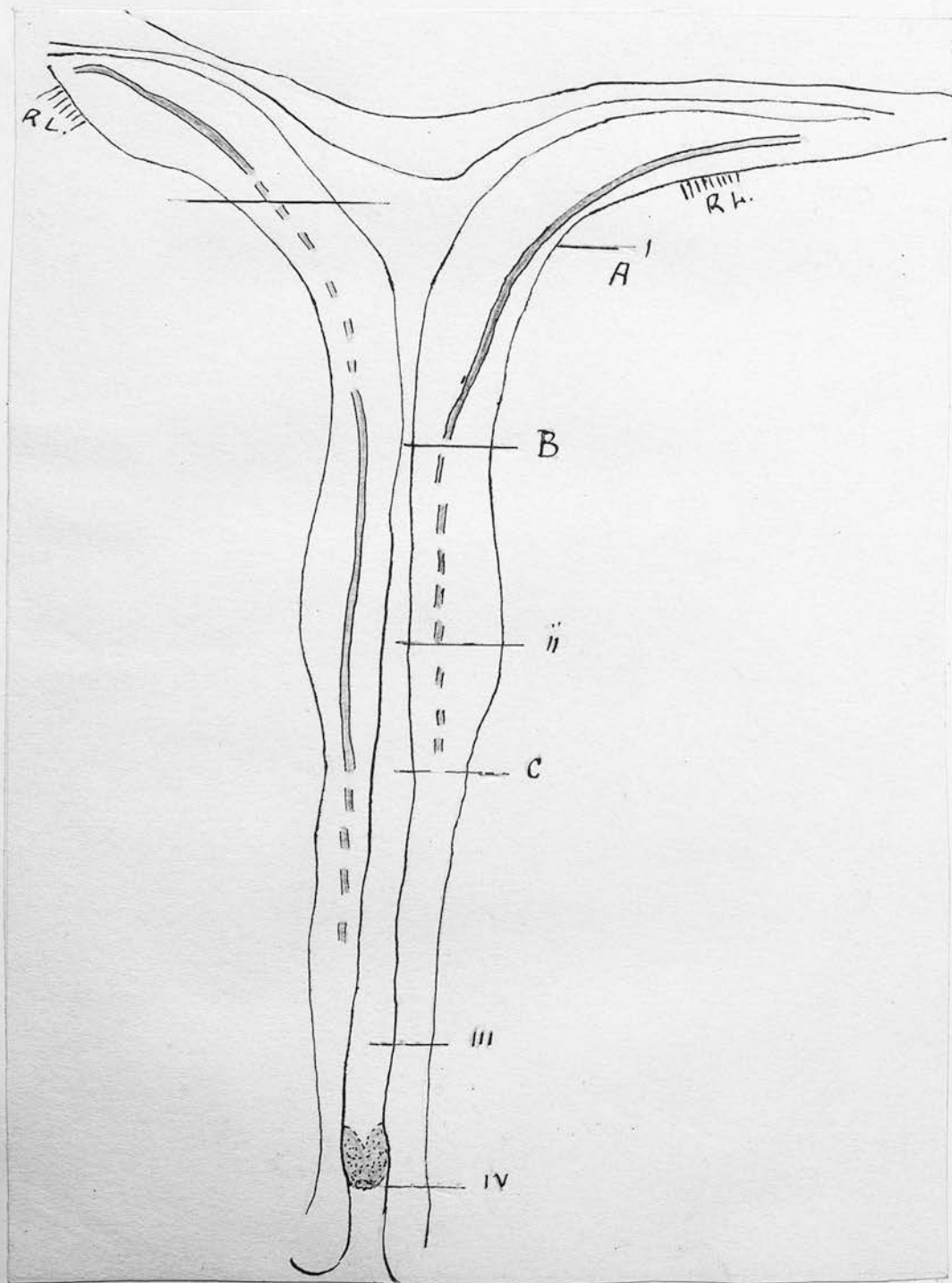


Fig. 35. 48 mm. embryo x 48 Reconstructions from the front (uv.) = utero-ventral cavity (W.D.) Wolffian duct (R.L.) = round ligament.

Utero-Vaginal Canal.

The Müllerian ducts have been seen to fuse proximal to the urogenital sinus. The fusion so produced constitutes the utero-vaginal canal, the gradual development of which must now be traced through further stages.

Embryo 48mm Utero-vaginal canal. As the ducts approach each other in this specimen, the tubar mesenteries come to fuse in the mid line to form a well developed Broad Ligament. With the approximation of the ducts the, here, lightly defined circularly arranged cells surrounding them give the temporary appearance of a median raphe. This appearance is soon lost: surrounded by a common mesodermic condensation, the ducts almost immediately fusing to form a single utero-vaginal canal.

The single cavity so formed, is elongated in its transverse axis, and lies in the band of mesodermic condensation before mentioned, this band being now much contracted laterally to form a compact mass round the utero-vaginal canal.

The cells forming this condensation, tend to be arranged round the cavity, in an inner and outer circular, and intermediate longitudinal layer - (see Fig.36) ^{note 14} but the arrangement is not very well marked. There is an area of increased condensation at the apices or lateral angles of the mesodermic structure, where the Wolffian ducts are seen surrounded by a circular layer of cells.

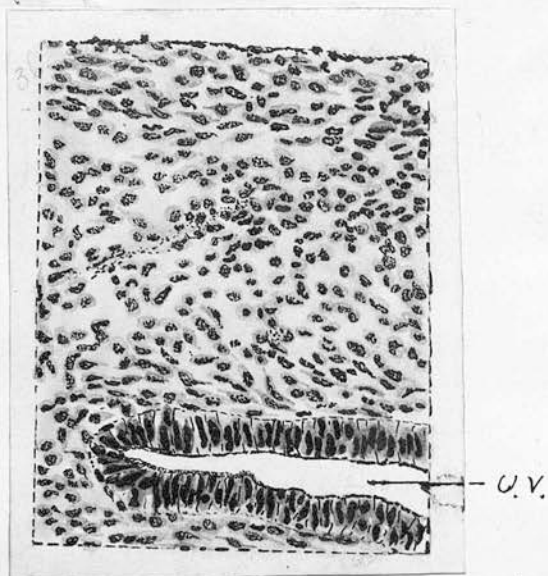


Fig. 36. 48 mm. embryo x 320 Proximal part utero-vaginal cavity, (uv.) level i Fig. 35.

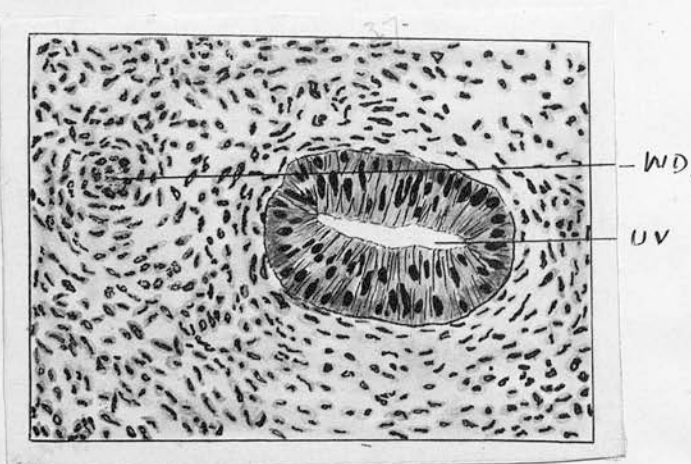


Fig. 37. 48 mm. embryo x 320. More distal "cervical" part of uterovaginal cavity (uv.), level ii Fig. 35. (W.D.)= Wolffian duct.

The lumen of the utero-vaginal canal shows a somewhat undulating outline and is lined by columnar epithelium lying on a well defined basement membrane. (See Level A. Fig. 35 and Fig. 36).

Followed caudally the cavity narrows gradually in its transverse, and later in its antero-posterior diameter, until the lumen is reduced to a mere slit. There is at the same time, a symmetrical narrowing of the surrounding mesodermic condensation, which becomes more cylindrical in shape, and the Wolffian ducts, which formerly lay in contact with its outer (lateral) borders, can now be traced into its substance. (See Level B. Fig. 35). The lining of this very narrow portion ? cervix of the canal, consists of high columnar epithelium lying in a very well marked basement membrane (see Fig. 37). This epithelium is definitely taller in character than that lining the more cephalic portion of the canal - the transition from one type to the other taking place gradually.

The cells in contact with the basement membrane here, are arranged circularly but beyond this an even less regular cell arrangement than previously is present, the cells on the whole tending to surround the blood vessels which are very numerous.

The Wolffian ducts gradually penetrate towards the lumen of the utero-vaginal canal surrounded by a well marked zone of cells arranged circularly.

Caudal to this, (see Level C. Fig. 35), the canal again widens laterally, the columnar epithelium becoming slightly lower in character, this change taking place rather

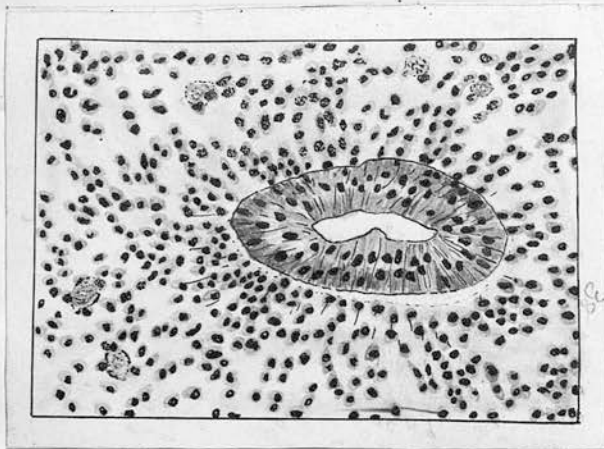


FIG. 38.

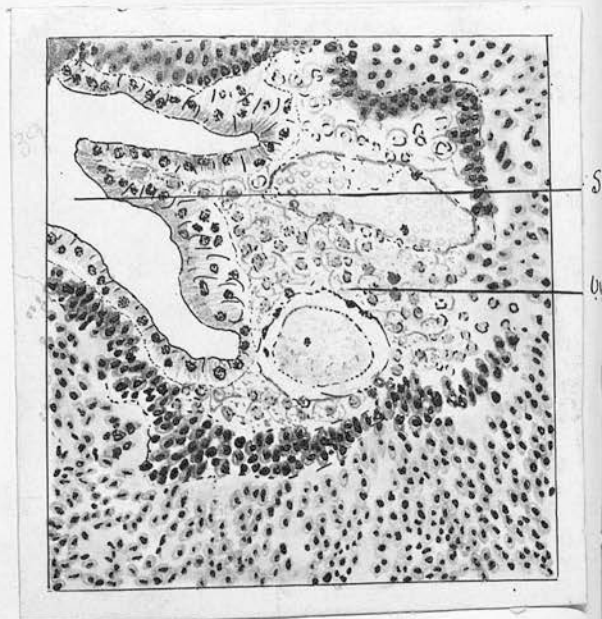


FIG. 39.

Figs. 38 and 39. 48 mm. embryo c 320. Sections of utero-vaginal canal levels iii and iv in Fig. 39 (S) - Sinus (u.v.b.) - Utero-vaginal

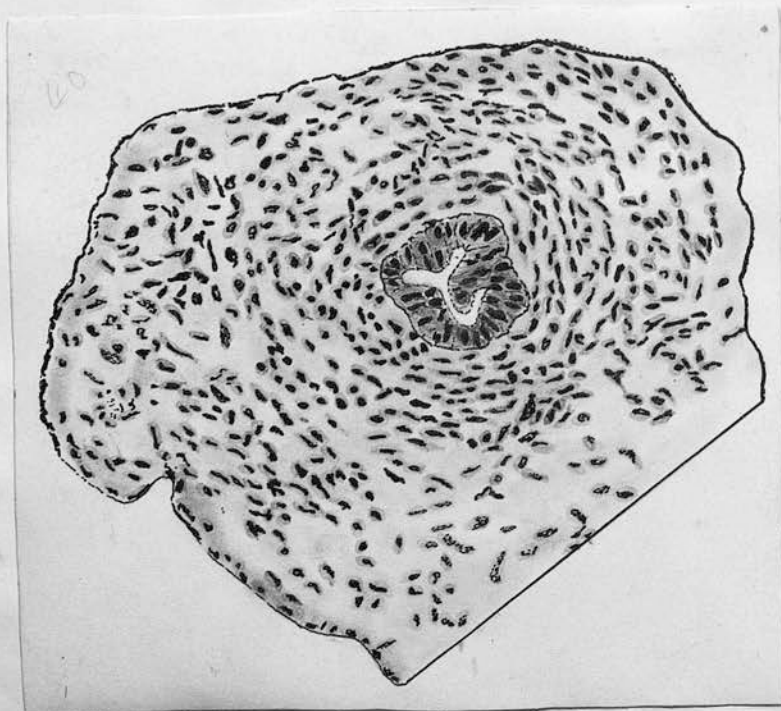


Fig. 40. 48 mm. x 320. Transverse section Fallopian tu

rapidly, while the layer of immediately subjacent circularly placed cells is replaced by a layer of much less condensed mesoderm.

The cells of this latter are arranged round the epithelium somewhat radially - but externally and irregular arrangement is again assumed.

The lumen of the canal here, is somewhat crescentic in outline, the interior of the posterior wall exhibiting rather irregularly placed grooves and ridges - some 2-3 in number.

As the utero-vaginal canal approaches the posterior wall of the urogenital cavity, it again diminishes in its long axis, the radial arrangement of its surrounding cells becomes much more marked and the cells lining it appear multilayered (see Fig. 38).

The narrowing of the lumen progresses by approximation and thickening of its walls, until the canal is reduced to a solid bar of cells possessing a potential cavity only. This solid epithelial bar pushes its way towards the dorsal wall of the sinus ? compressing the intervening mesoderm, which is here much more compressed than elsewhere, until it abuts on the sinus epithelium ? breaking through the cells of the submucous or basement layer, but not through the sinus epithelium proper which is pushed forward by the growing bud of utero-vaginal, which again assumes a fairly definite bi-lobed appearance, degeneration of some of its cells giving rise to ? double lumen (see Fig. 39). This epithelium pushes its way for some 5-6 10u sections along

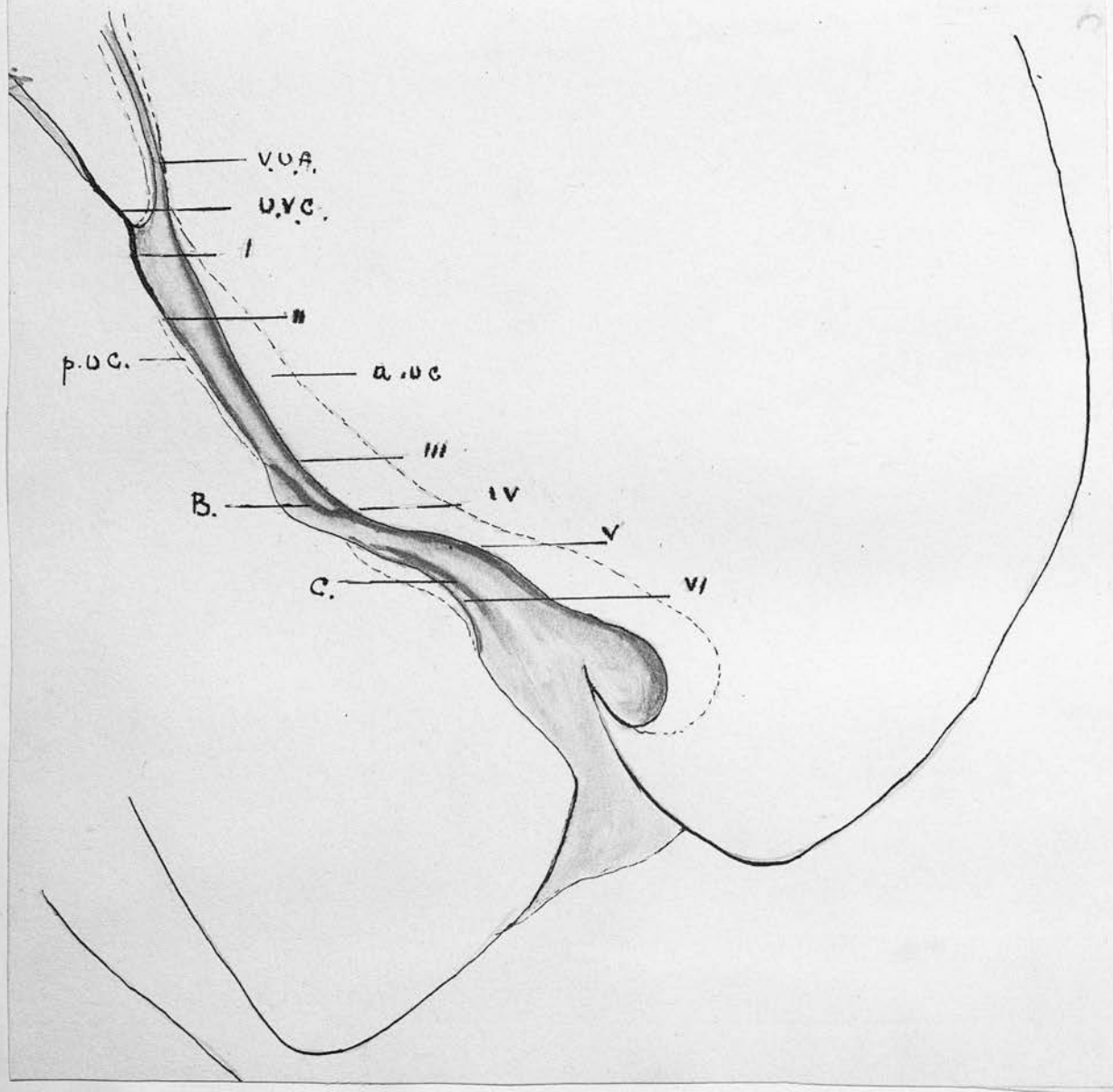


FIG. 41.

Figs 41, 42, and 43.

48 mm embryo x 50
 Sinus (41) and (43) - seen from the front, (43)
 with ant. urog. crest cut away - (42) transverse
 sections at levels i, ii, iii, iv, v, vi, (v.u.a)
 = vesico urethral anlage, (u.v.c.) utero-vaginal
 canal, (a.u.c.) = ant. urogenital crest, (p.u.c)
 = post urogenital crest, (B) = Bartholin's groove,
 (Bo) = orifice of Bartholin's duct, (A) and (C)
 = grooves "A" and "C".



FIG. 42.

the posterior wall of the urogenital sinus.

The tube in this stage shows many developmental advances. The ostium abdominal possesses small simple fimbriae, one on the left side being larger specially well marked ? fimbria ovarica.

Within the lumen of the outer part of the tube irregular heaping up of the epithelium, gives the interior a slightly rugose appearance, but the epithelium folds possess no mesodermic supporting core (see Fig.40). The tube possesses a well marked surrounding mesodermic condensation - the cells immediately underlying the tall columnar epithelial lining being grouped to form a well defined circular layer.

Note. I have above given the description of the developing utero-vaginal canal at this stage, in very great detail. In the immediately following specimens described it will suffice to note changes and modifications together with developmental advances.

Sinus 48. (See Figs. 41, 42 and 43).

General Description. Little change has taken place in the general contours and relations of the sinus since the last stage. The Pars pelvina is still long and narrow relatively to the pars phallica.

The solid utero-vaginal epithelial reaches the posterior wall of the sinus, but only invaginates this to a slight degree, Müller's tubercle being in consequence, poorly marked. The relief of the inner aspect of the sinus walls is becoming rather more complicated and Bartholin's groove is now deep and well marked. Definite acini are present in Bartholin's gland which opens by a duct into Bartholin's groove.

The utero-vaginal epithelial bud extends a little way caudally on the posterior sinus wall.

Detailed Description.

The solid vaginal epithelial bud makes contact with the posterior aspect of the urogenital sinus which at this level possesses a low anterior urogenital crest. (Level i. Figs. 41, 42 and 43).

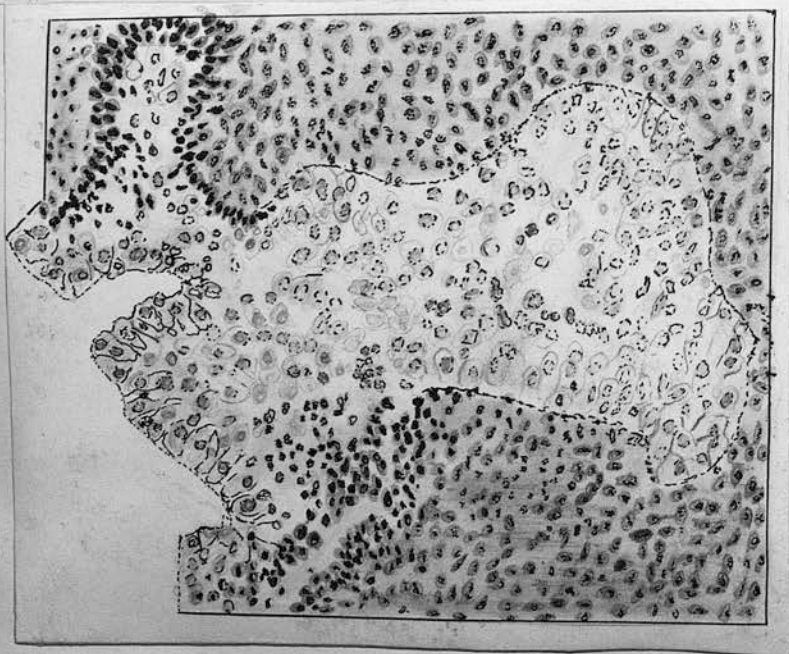
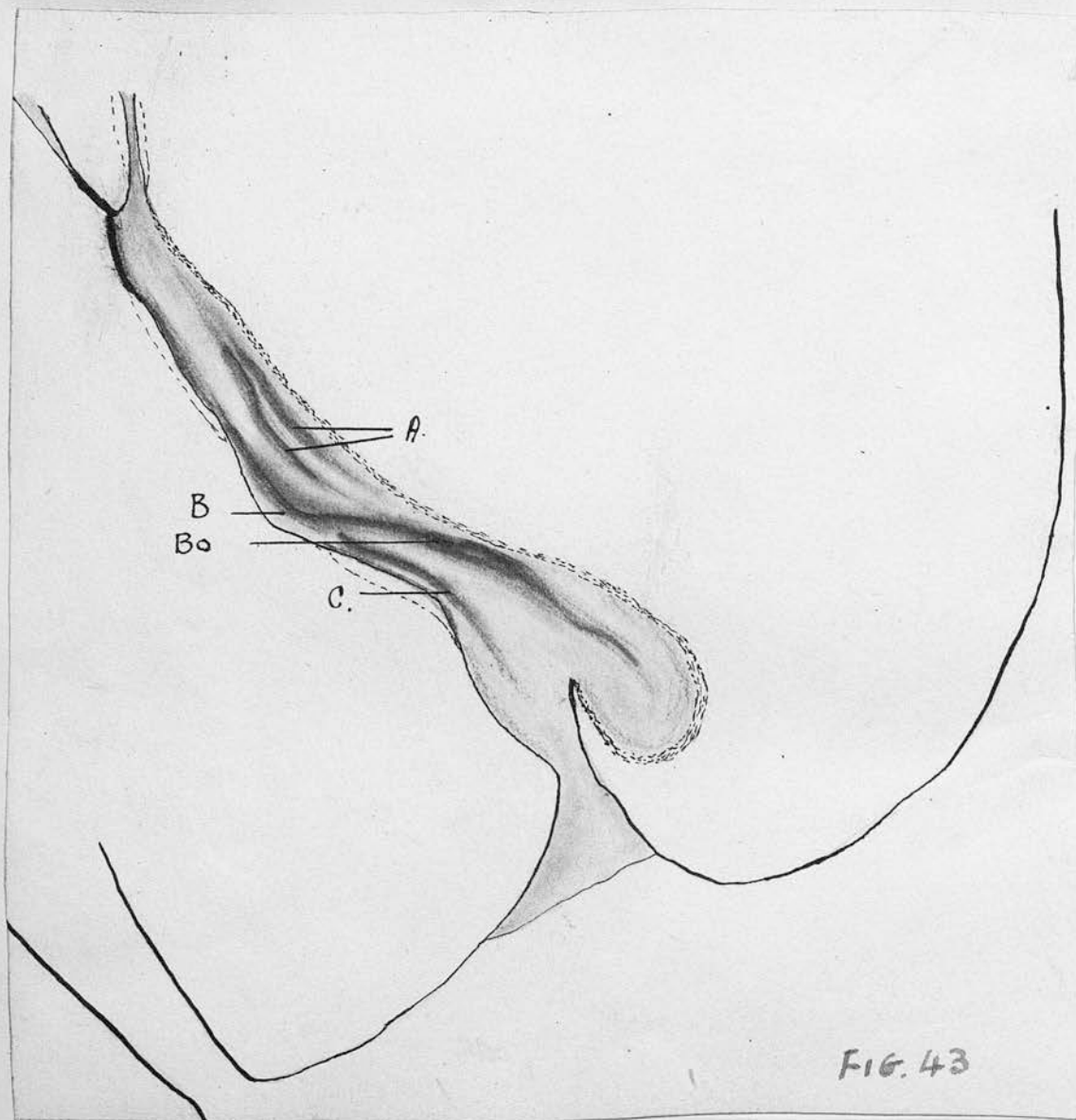


Fig. 44.

55 mm. embryo x 320

Utero-vaginal epithelial bud making contact with sinus epithelium

Following the sinus caudally, a low posterior urogenital crest develops which has epithelial indentations on its apex and is flanked on either side by a well-marked postero-lateral groove. On either side of the anterior urogenital crest are deep anterior lateral grooves (Level ii. Figs. 41, 42, 43).

The epithelium on the posterior urogenital crest gives place to a shallow posterior urogenital recess. The antero-lateral grooves deepen, possessing medial and lateral walls. On the lateral wall of the antero-lateral groove, shallow longitudinally - placed second grooves develop. Examination of older specimens show these to be constant in appearance, and will henceforth be known as the grooves (A), (A1) & etc. (see levels iii. Figs. 41, 42, 43).

The postero-lateral grooves deepen, and their outer extremities become bifid. Bartholin's gland and duct is present as an epithelial budding from this anterior limb of the postero-lateral groove (B) which is considerably deeper than in former specimens (see levels iv, v. Figs. 41, 42, 43).

The antero-lateral groove continues to deepen with corresponding prominence of the anterior urogenital crest, while a low posterior urogenital crest again appears in the base of the posterior recess - the lateral walls of which show a poorly marked longitudinal groove (C)

The bifid character of the groove (B) is gradually lost, the groove being directed downwards to gradually open out beneath the anterior urogenital crest (see levels vi. and vii. Figs. 41, 42, 43).

Embryo 55mm. Utero-vaginal canal.

Only the lower or caudal portion of the utero-vaginal canal is included in this specimen. The canal is lined by high columnar epithelium, and has here a crescentrically shaped lumen, which is surrounded by a well marked capsule of condensed mesoderm in the substance of which on the right side a segment of Wolffian duct can be recognised. This possesses here a well marked lumen surrounded by a layer of circularly placed cells.

Traced caudally the canal runs with a gentle cavity directed forwards, and becomes first oval, then slit-like in shape, its anterior and posterior walls thickening

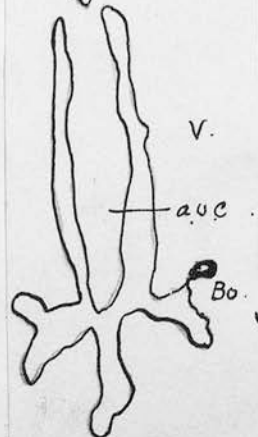
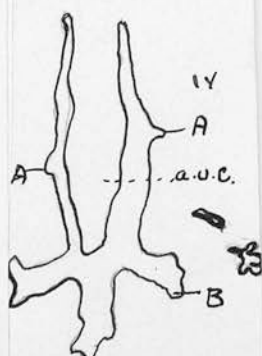
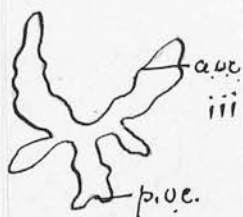
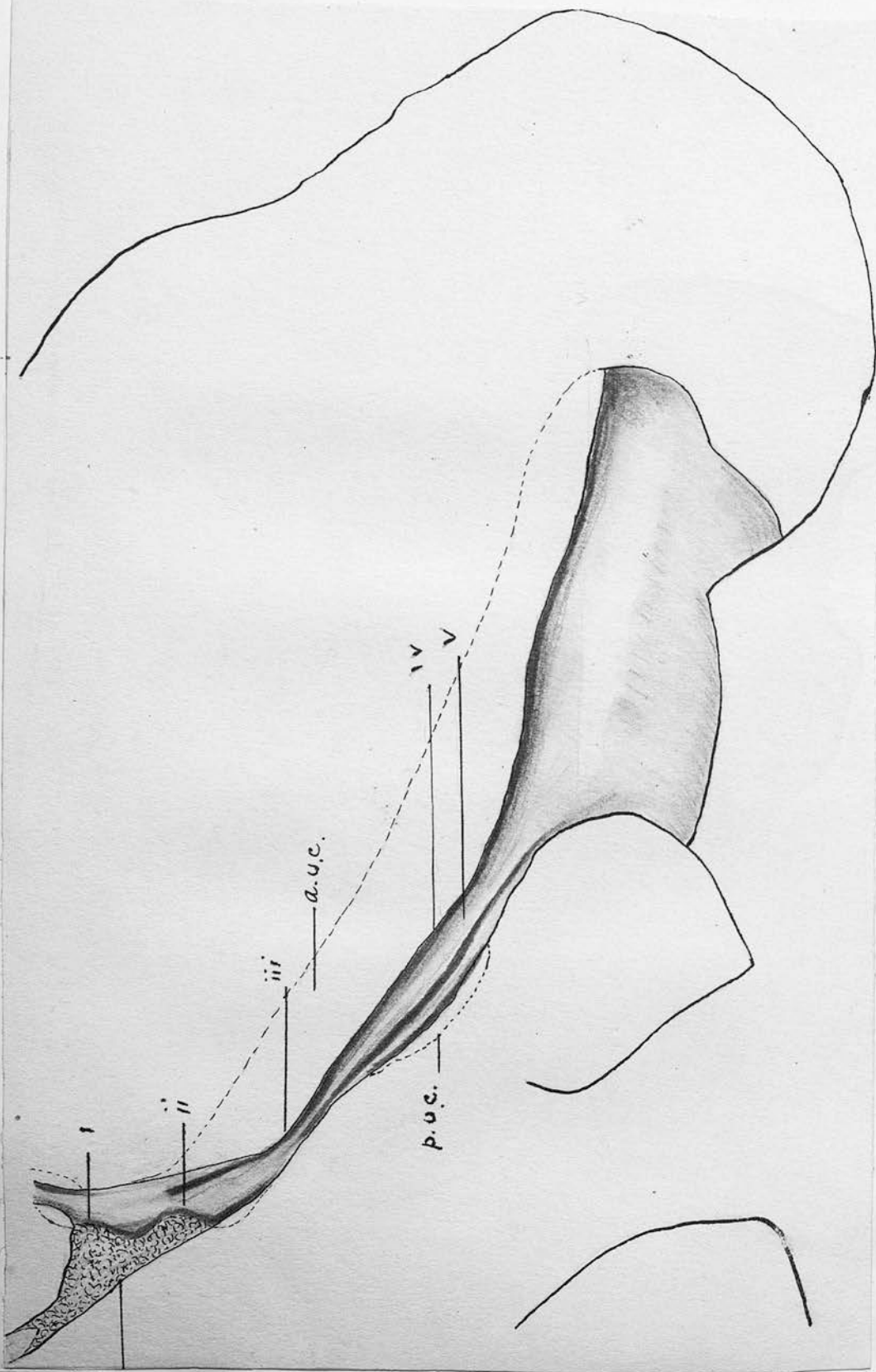


Fig. 46.

Fig. 45.

Figs. 45, 46 and 47. 48 mm. embryo x 50 (45) and (47) = reconstruction of sinus seen from the side, (47) with ant. urogenital crest removed (46) = transverse sections at levels i, ii, iii, iv, v, in Fig. 45 and 47 (u.v.b.) = utero-vaginal bud, (a.u.c.) = Ant. urogenital crest, (p.u.c.) = post urogenital crest, (B) = Bartholin's groove (Bo) = orifice of Bartholin's duct, (A) = Grooves "A" (C) = Grooves "C"

through proliferation, and coming into contact with each other, this process commencing at the external angles.

By this means the utero-vaginal canal is reduced to a solid column of cells, which gradually assumes a triangular or triradiate shape. The anterior process of this mass grows out towards the dorsal wall of the urogenital sinus, with which it at length comes into contact, invaginating it, and growing for a short distance along its posterior aspect. No communication, however, exists at this stage between the utero-vaginal epithelial mass and the sinus lumen (see Fig. 44).

Sinus 55mm. (see Figs 45, 46 and 47).

General Description. There is here a persistence of the long narrow pars pelvina of the sinus. The solid utero-vaginal bulb forms a low Müllerian tubercle, by invaginating the posterior wall of the urogenital sinus, along which the epithelium grows caudally for a short distance.

The anterior urogenital crest is very prominent, and under cover of it lies the shallow groove (A). Bartholin's groove (B) is deep and well marked, and Bartholin's duct opens into it about the junction of the pars pelvina and pars phallica. A small posterior urogenital recess is present, showing a shallow groove (C) on its lateral walls. A low posterior urogenital crest develops caudal to this level.

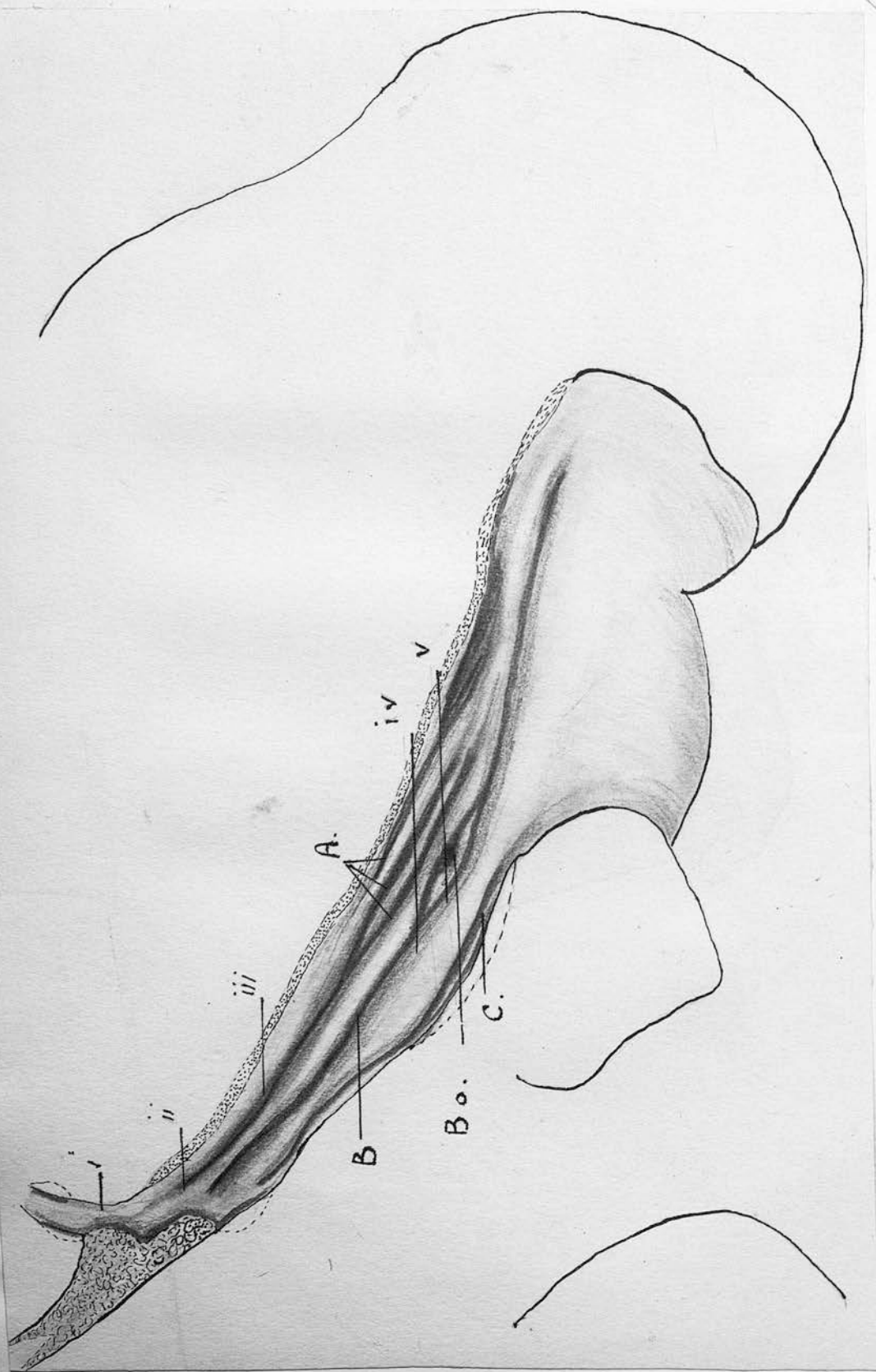


FIG. 47.

Detailed Description. The utero-vaginal canal is solid in its caudal part, and comes into contact with the posterior sinus wall, invaginating this slightly, and extending along it distally for some little way.

Shortly distal to this area of contact, a low anterior urogenital crest appears; while, lying in the lateral wall of the sinus at this level, is the beginning of a groove, which study of serial sections shows to be the groove (B) (see levels i, ii. Figs 45, 46 and 47.)

Continuing caudally, - a small epithelium-lined recess - the posterior urogenital recess - is seen to develop at the area of contact between the utero-vaginal epithelial downgrowth and the posterior sinus wall. At the same level the anterior urogenital crest becomes much more prominent being demarcated by deep antero-lateral grooves, which carry secondary longitudinal grooves (A) on their lateral walls. Bartholin's groove becomes deeper and more distinct, and, lying here more or less in the long axis of the sinus, passes under cover of the antero-urogenital crest (see levels iii, iv and v. Figs. 45, 46 and 47).

The small posterior urogenital crest shows the presence of its mural groove (C) and later a low posterior urogenital crest. Bartholin's groove deepens and its external extremity becomes bifid. Bartholin's duct and gland arise from the anterior limb of the bifurcation.

Embryo 65mm.

Utero-vaginal Canal. (See Fig. 48).

The union of the Fallopian tubes here does not exhibit any point of special interest. The utero-vaginal canal so formed is surrounded by a well-marked area of mesodermic condensation in which the arrangement of the cells appears to be quite irregular.

The cavity is lined by low cubical epithelium. The histological preservation of this specimen is poor, making changes in the type of epithelial lining cells difficult

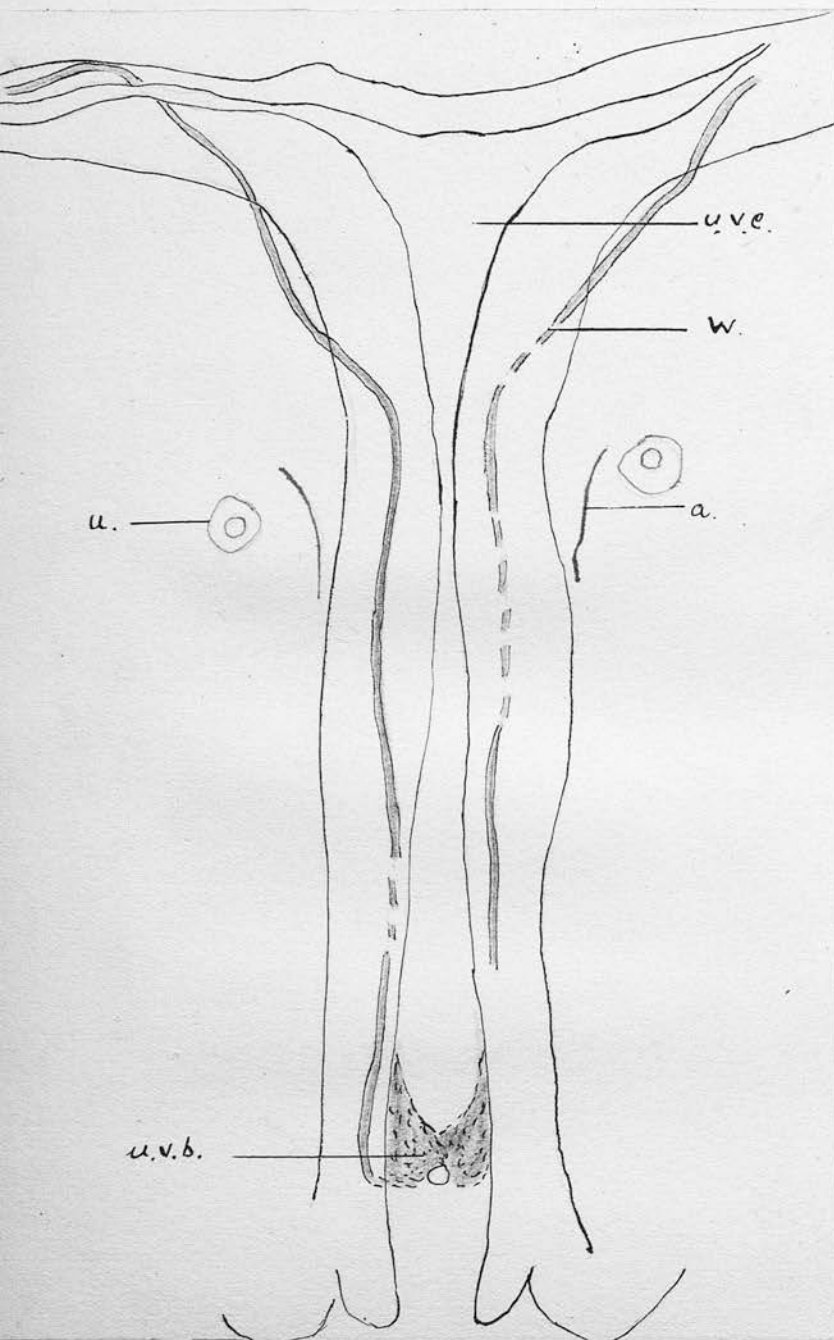


Fig. 48.

65 mm. embryo x 35 Reconstruction of utero-vaginal canal seen from the front (u.v.c.) = utero-vaginal canal, (W) = Wolffian duct (a) = Uterine artery (u) = ureter (u.v.b.) = utero-vaginal epithelial bud.

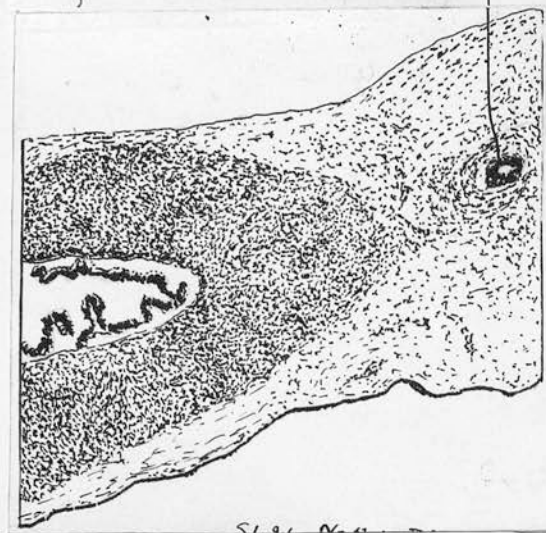


Fig. 49.

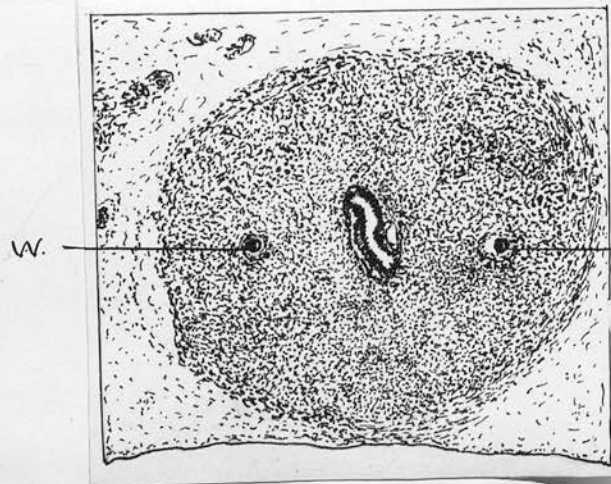


FIG. 50.

Figs. 49 and 50.

65 mm. embryo x 70. (49) section through proximal part of utero-vaginal canal. (50) section through more distal part of utero-vaginal canal. (W) = Wolffian duct.

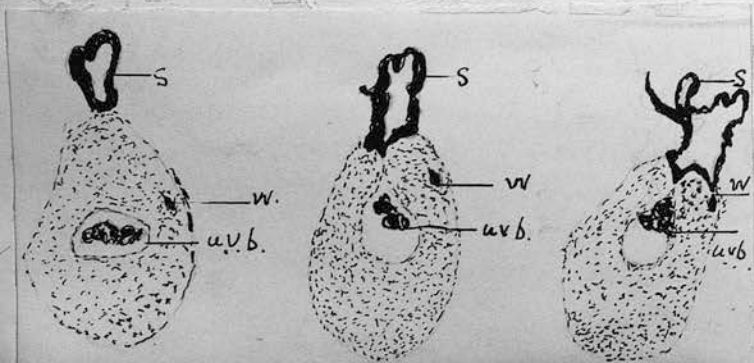


Fig. 51.

65 mm. embryo x 30. To show Wolffian duct = (W) entering sinus (S), distinct from utero-vaginal bud = (u.v.b.)

of detection, but it appears that the mucous membrane exhibits small folds which, in the caudal portion of the canal, are two in number, anterior and posterior, and give the interior of the canal a somewhat wavy outline. These little folds affect the epithelial layer only and are unsupported by the underlying mesoderm (see Fig. 49).

Segments of the Wolffian ducts can be picked up at intervals in the caudal part of their course, and are found running within the mesoderm surrounding - and are gradually approximating to - the utero-vaginal canal (see Fig. 50).

The utero-vaginal canal narrows as it is followed caudally and becomes solid by the filling of its lumen with epithelial cells. The epithelial mass so formed sends out an anterior prolongation or process which comes into contact with and bulges the posterior sinus wall (a short segment of the right Wolffian Duct can be here picked up near the lateral angle of the utero-vaginal canal). Just caudal to this point the right Wolffian duct can be seen to enter the sinus, lateral to, and quite independent of, the utero-vaginal epithelial mass which sends an epithelial downgrowth or bulb along the posterior wall of the sinus (see Fig. 51).

The tube does not as yet show the presence of true fimbriae at its abdominal end, but possesses an ostium with a very definite thinned out lateral and median lip, the latter of which is directed towards the ovarian hilum and is supported by a slightly condensed mesodermic tissue continuous with that of the tube wall. The lining cells of the tube are slightly heaped up

Figs. 52 and 53.
 65 mm. embryo x
 70. Fallopian
 tube. (52) = ab-
 dominal ostium.



Fig. 52.

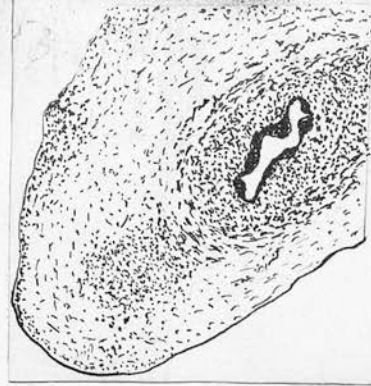
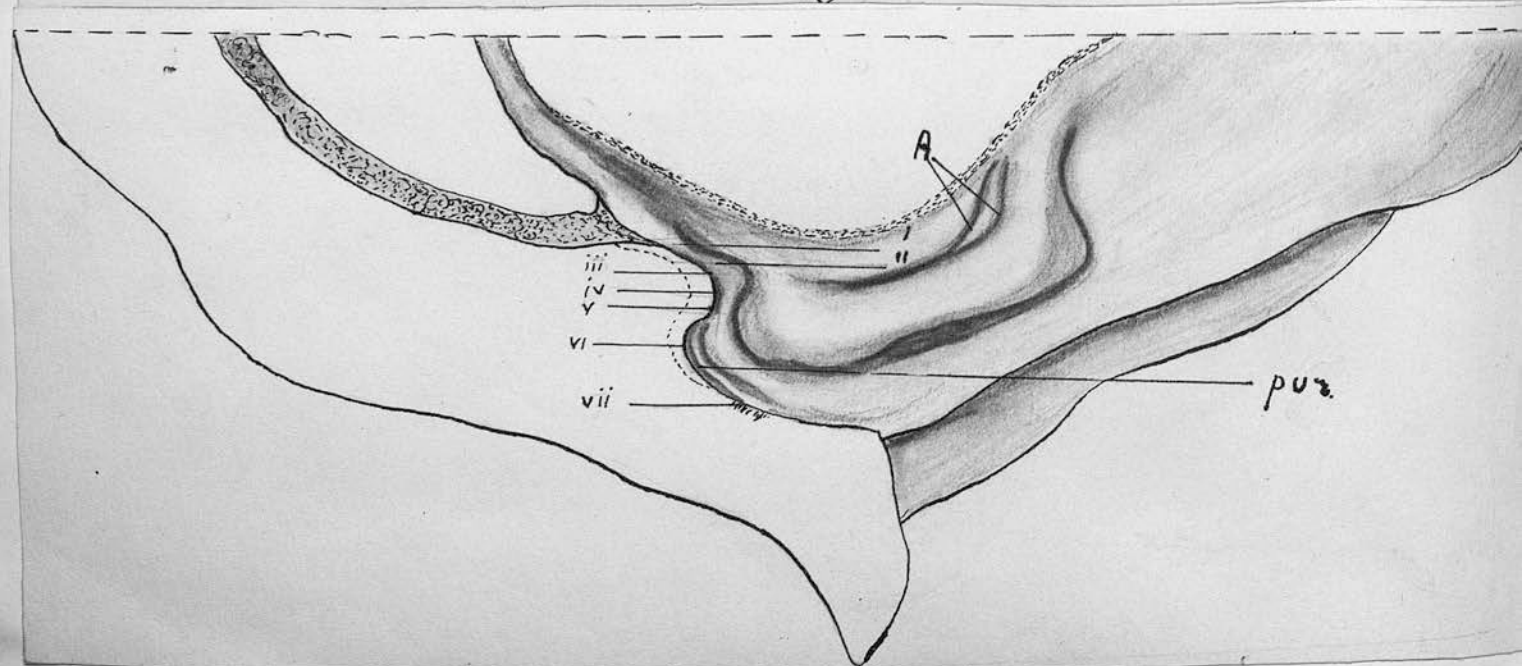
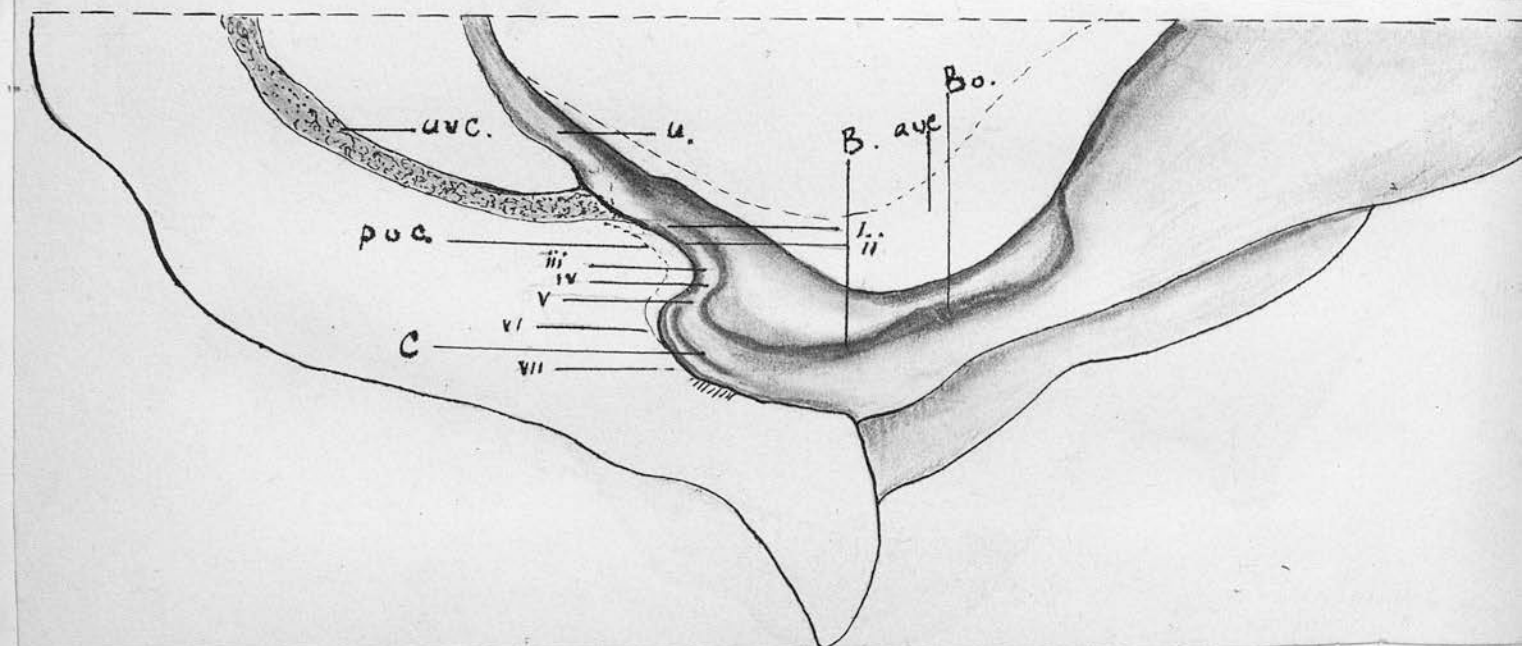


Fig. 53.



Figs. 54 and 55.

locally, but form no true tubal folds. As in former specimens the tube runs a somewhat wavy and undulating course and possesses like the last specimen a wall containing a well-marked circular but no longitudinal layer (see Figs. 52 and 53).

Sinus 65mm. (See Figs. 54, 55 and 56).

General Description. The pars pelvina of the sinus in this specimen shows a great relative and absolute diminution in length in comparison with the pars phallica, which is here short and wide. The solid utero-vaginal bud reaches the posterior sinus wall, but little invagination of this is present.

The anterior urogenital crest is prominent, and the groove (A) under cover of it, short but well marked. Bartholin's groove is deep and, being bent on itself by the invagination of the posterior sinus wall, forms a wide angle, the anterior part only being under cover of the anterior urogenital crest. A small posterior urogenital recess and crest are present.

Detailed Description. The utero-vaginal bud at its area of contact with the posterior sinus wall, here invaginates this slightly. Lying postero-lateral and just distal to the area of contact of the utero-vaginal canal and sinus, the Wolffian duct can be seen entering the sinus in the groove formed by the forward bulging of the posterior wall. The sinus here shows a very deep prominent anterior urogenital crest, under cover of which the pars pelvina joins the pars phallica at somewhat of an angle (see levels i and ii. Figs. 54, 55 and 56).

The epithelium of the utero-vaginal bud extends caudally some little way along the posterior sinus wall. A small posterior urogenital recess is present, with a low posterior urogenital crest, and later having a longitudinal shallow groove (C) in its lateral wall. Bartholin's groove (B) extends from a little

Figs. 54, 55 and 56.

65 mm. embryo x 30. (54) and (55) - reconstructions of sinus seen from the side (55) after removal of ant. urogenital crest. (56) = transverse sections at levels i, ii, iii, iv, v, vi, vii in Figs. 54 and 55. (u) = urethra, (u.v.c.) = Utero-vaginal canal, (a.u.c.) = Ant. urogenital crest, (p.u.c.) = post urogenital crest, (p.u.r.) = post urogenital recess. (B) Bartholin's groove (B.o.) = orifice of Bartholin's duct (A) = groove "A" (C) = groove "C"

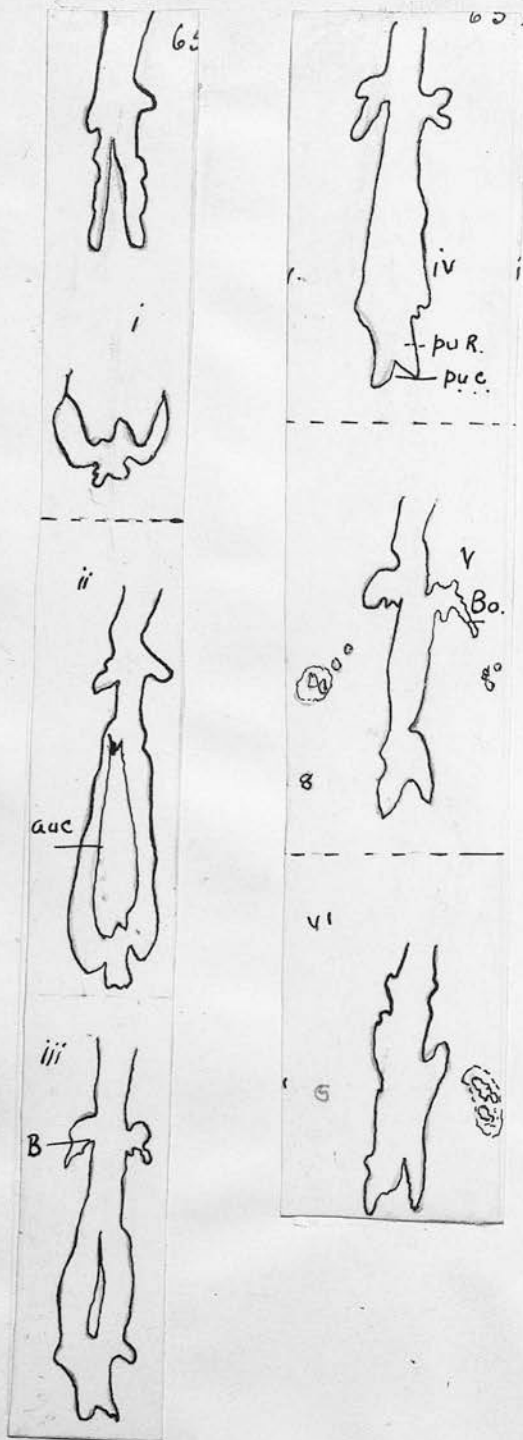


Fig. 56.

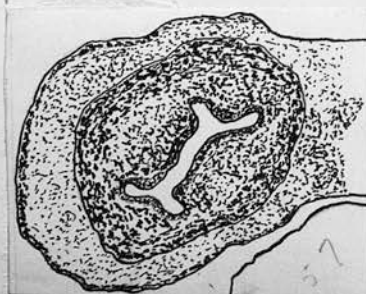


Fig. 57. 79 mm. embryo x 74. Trans. section Fallopian tube

caudal to the utero-vaginal sinus junction, and is slightly angled, the posterior part being shallow, and the anterior limb deeper and lying at first beneath the anterior urogenital crest, where the shallow groove (A) described in former specimens can also be made out. Bartholin's groove, especially in its anterior part, deepens to form a marked epithelial-lined recess (see levels iii, iv, v, vi, vii. Figs. 54, 55 and 56).

Embryo 79mm.

Tube. The abdominal ostium of the tube in this specimen shows no definite fimbriae but antero-medial and postero-lateral lips are present. The tube, from its inception, appears to have a definitely rugose lining, the folds consisting of mucous and submucous layers, supported by a fine mesodermic ingrowth from the surrounding condensation. This arrangement of folds in the wall of the tube, can be traced over several consecutive sections, the lumen of the tube assuming a somewhat quadriradiate shape, which is gradually lost sight of as the tubes approach each other in the mid line (see Fig. 57).

No other point of special interest is to be noticed.

The combined utero-vaginal cavity (see Fig. 58), as far as can be seen (the histological condition of the specimen is poor) has a lining possessing definite folds, but as yet no evidence of glands. The cavity is surrounded by a well marked mesodermic condensation, the cells of which are arranged in an inner, loose, very vascular, reticular and longitudinal layer, with

an outer layer of circularly arranged cells.

As the cavity is traced distally the arrangement of its lining mucosa becomes simplified and the epithelium is of a high columnar character.

By a process of epithelial hypertrophy, and approximation of its anterior and posterior walls - which commences laterally and extends medially - the simple epithelium lined utero-vaginal tube is reduced to a solid bar of cells. As we have noticed, the central fact up to this stage, is the evidence of a certain amount of activity in the Müllerian derivatives at this level - i.e. at and for a little distance above their area of contact with the sinus. In this 79mm specimen is seen the beginning of a further and definite evolution in this activity. Here the epithelial proliferation at the lower part of the utero-vaginal canal has assumed certain definite characters, progressing mainly at their "centres", which, however, are naturally continuous. Of these, two are laterally, and the third, centrally placed, so that three bulbous swellings of irregular outlines are produced. The lateral "bulbs" are somewhat larger than the central one, which projects more like a keel on the front surface, and makes the contact with the wall of the sinus. The cells forming these bulbs assume a somewhat concentric arrangement, the innermost cells becoming large, rounded, and vacuolated, with a tendency to break down, the whole bulb giving the impression on section of a "cell nest". Although there are three main

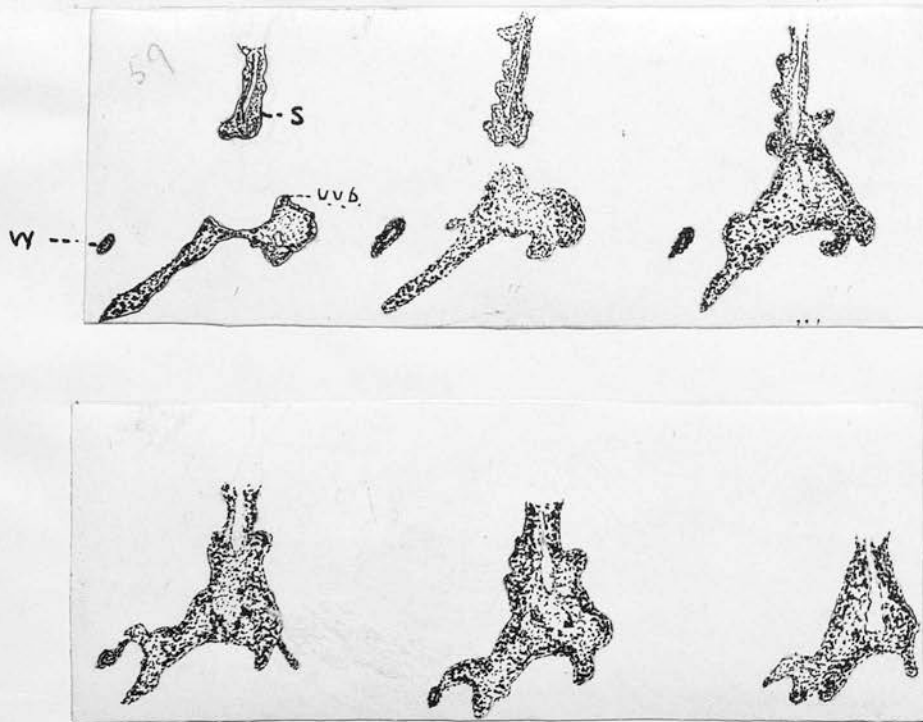


Fig. 59 79 mm. embryo x 50 serial sections to show Wolffian duct (W) coming into contact with utero-vaginal epithelial bud (u.v.b.) (S) = sinus.

centres, it must be understood that there are many small and separate ones as well. The area of this growth extends for a considerable distance up the vaginal canal.

The triradiate or T-shaped form of the vaginal mass, as seen on section, and mentioned in earlier stages, is preserved in this, the definite bulbous formations being essentially only further elaborations of the former central and lateral thickenings.

In this particular specimen, there is an interesting condition to be noted. The Wolffian duct, on the left side, which can be traced as a patent tube for some sections above the level mainly concerned in the description just given, can be seen to come into direct contact, lower down, with the outer aspect of the left lateral vaginal bulb, but without in any way participating in the formation of this structure. (Fig. 59) gives the serial sections in which this occurs, and it can be seen that the remnant fades away without any sign of epithelial activity or bulb formation at its lower end. This is the only example we have in our specimens of a Wolffian duct coming close to, or in contact with, the Müllerian cells, and there seems to be no reason to doubt that the condition in this case is an accidental combination of a localised irregular growth of vaginal cells, with a persistent Wolffian remnant.

It will be remembered that it was shown in earl-

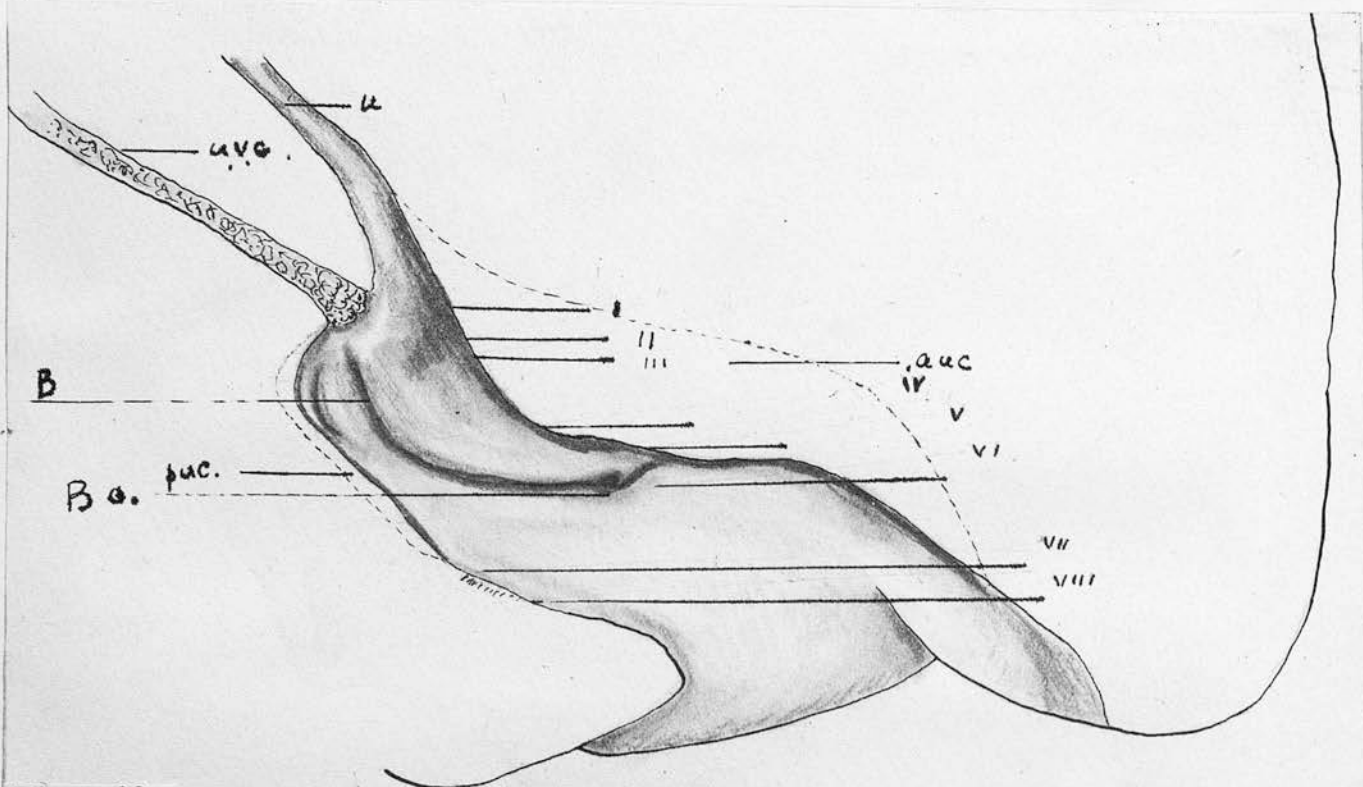


Fig. 60.

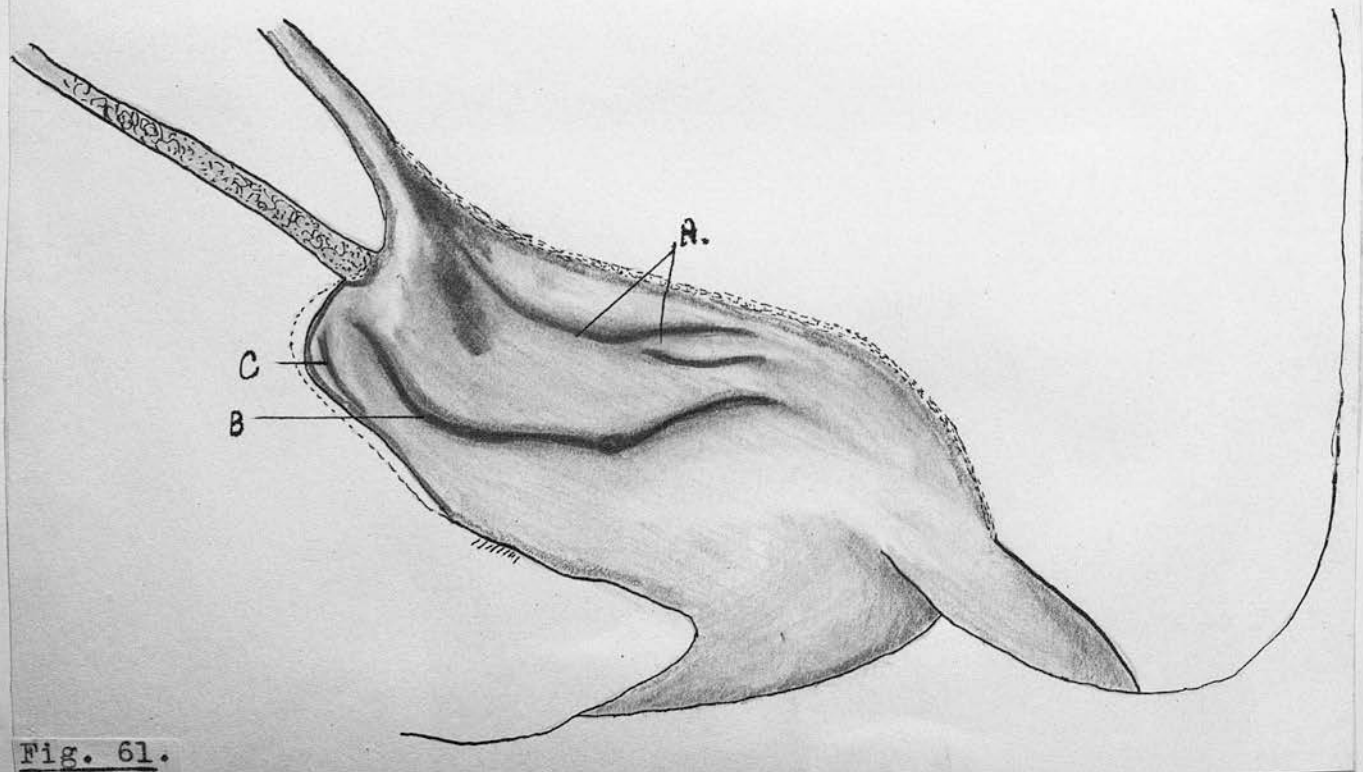


Fig. 61.

Figs. 60, 61, and 62. 79 mm. embryo x 20 (60) and (61) = Reconstruction of sinus seen from side (61) after removal of ant. urogenital crest (60). Transverse sections at levels, i, ii, iii, iv, v, vi, vii, viii = Figs. (60) and (61), (u.v.c.) = utero-vaginal canal, (u) = urethra, (a.u.c.) = ant. urogenital crest, (p.u.c.) = post urogenital crest, (B) = Bartholin's groove, (B.o) = orifice of Bartholin's duct, (C) = groove "C", (A) = grooves "A"

ier specimens that the utero-vaginal canal comes into contact by its epithelium with the upper and posterior wall of the urogenital sinus. It is by means of the vaginal bulbs, which have now been mentioned, that this area of contact is maintained and increased, the vaginal cells pushing their way, by this proliferation, downwards along the posterior wall of the sinus.

Sinus 79mm. (see Figs. 60, 61 & 62). The solid utero-vaginal canal comes into contact with the posterior sinus wall, by means of the anterior vaginal bulb just described.

At this level a very prominent anterior urogenital crest is present, underlying which are deep antero-lateral grooves. The anterior urogenital crest here shows some epithelial indentations into its substance, the meaning of which, are not quite clear but which are present in other specimens (see levels i, ii. Figs. 60, 61 and 62).

Under cover of the anterior urogenital crest, the longitudinal groove (A) makes its appearance, being here very well marked and forming a deep epithelial-lined fossa with an overhanging upper lip. It disappears more distally leaving smooth the walls of the deep antero-lateral grooves (see levels iii and iv Figs. 60, 61 and 62).

The posterior part of the urogenital sinus is prolonged slightly backwards to form a posterior urogenital recess, with posterior urogenital crest in its base (see levels iii and iv. Figs. 60, 61 and 62).

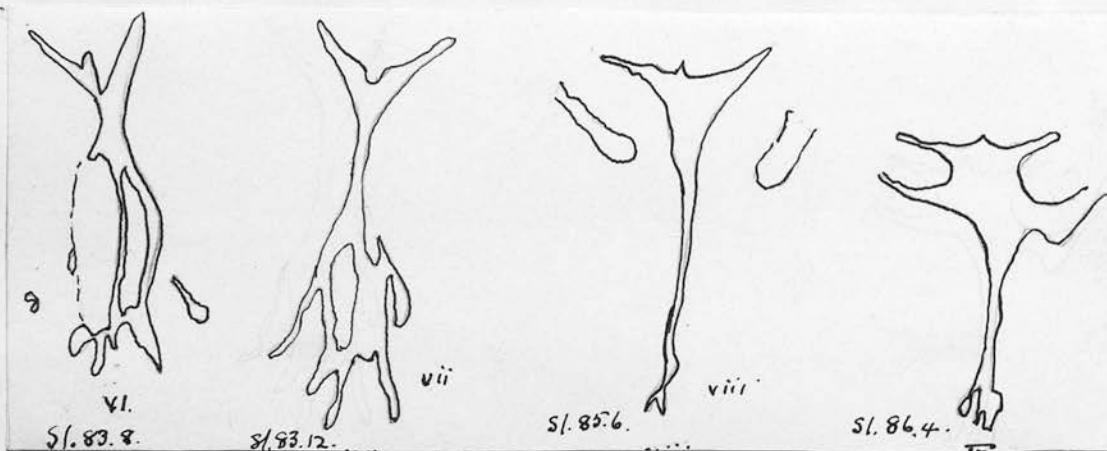
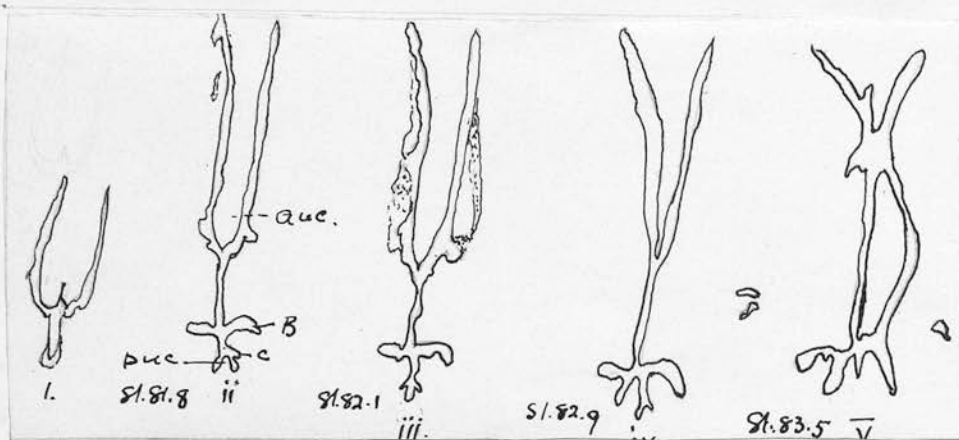


Fig. 62.

Fig. 63, 64 and

110 mm. en
bryo x 45.
Fallopian
tube (63).
abdominal
ostium, (65)
= inner en

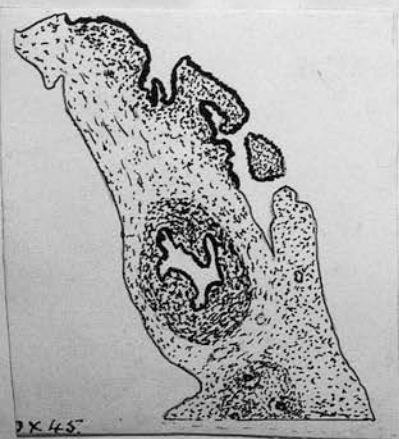


Fig. 63.

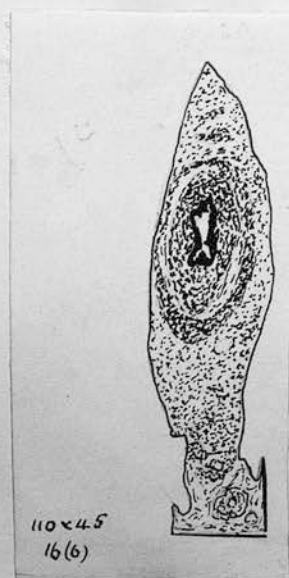


Fig. 64.

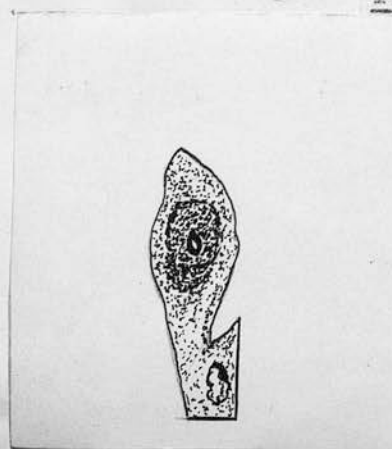


Fig. 65.

The groove (B) commences posteriorly in the lateral wall of this recess - and runs longitudinally as a well marked epithelium lined furrow. This deepens greatly, and becomes bifid at its outer extremity. From the anterior limb of this bifid extremity Bartholin's duct arises. Bartholin's groove in the sinus wall lies parallel to the groove (A) before mentioned - and under a similar overhanging shelf of epithelium - the relief of the lateral sinus wall in this specimen being much complicated by the presence of these deepened epithelial recesses with their overhanging lips (see levels v, vi, vii. Figs. 60, 61 and 62).

In the lower part of the posterior sinus wall some coarse epithelial ingrowths or indentations are present, the meaning of which are not quite clear but which are possibly pressure effects (see levels viii, ix. Figs. 60, 61, 62). The sinus is enclosed by a definite mesodermic condensation, continuous with that surrounding the vagina and Bartholin's glands.

It will be noticed here - see reconstruction - that great shortening and widening of the pars pelvina has taken place, and this, together with the approximation of the vaginal sinus area of contact to the mouth of Bartholin's duct which may be taken to be a fixed point, goes to prove that invagination of the posterior sinus wall is taking place. This change will be fully discussed later, when the factors bringing it about become more marked.

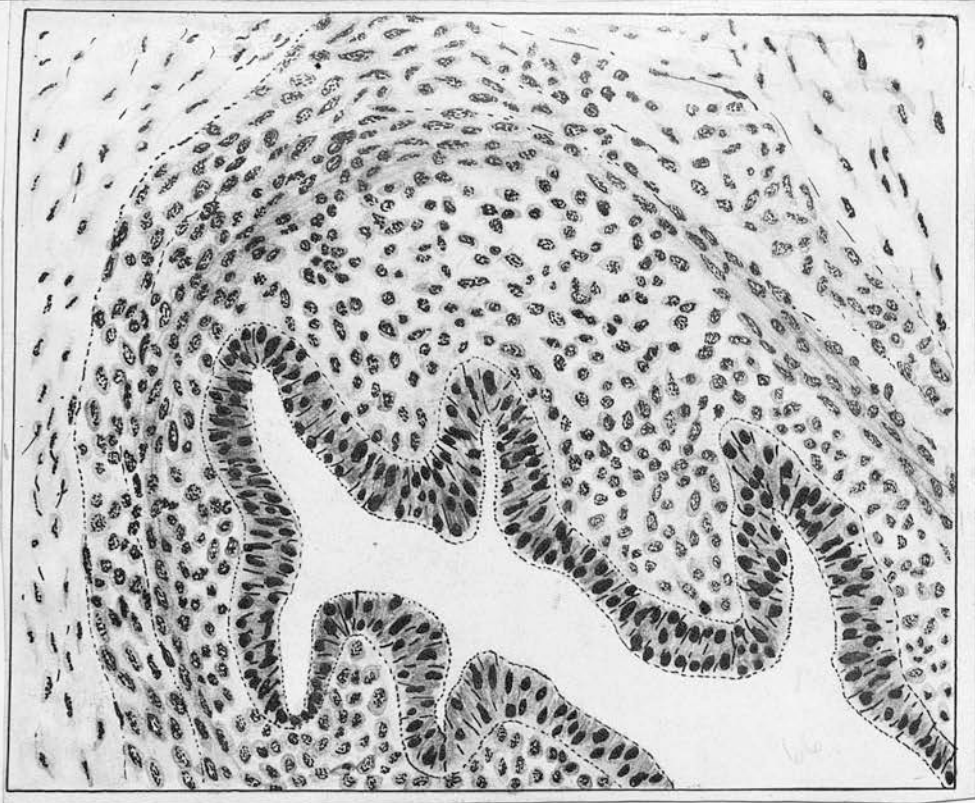
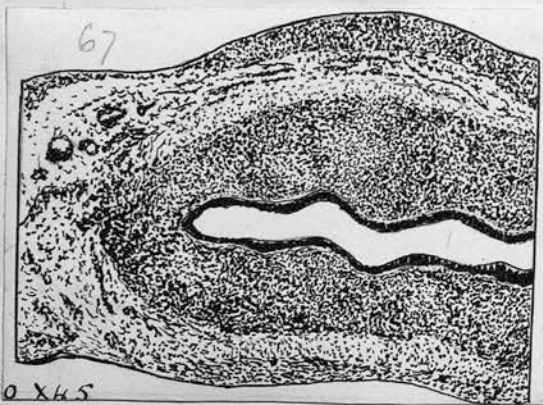


Fig. 66. 110 mm. embryo x 320. Fallopian tube to show histology of wall.



0 X45

Fig. 67.

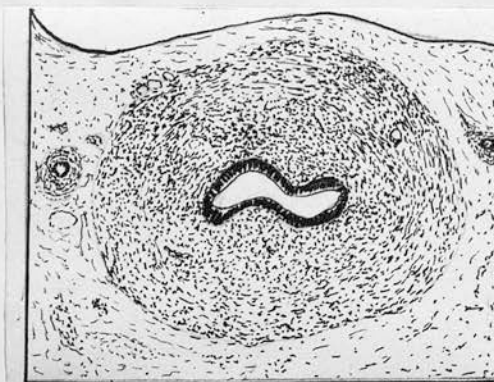


Fig. 68.

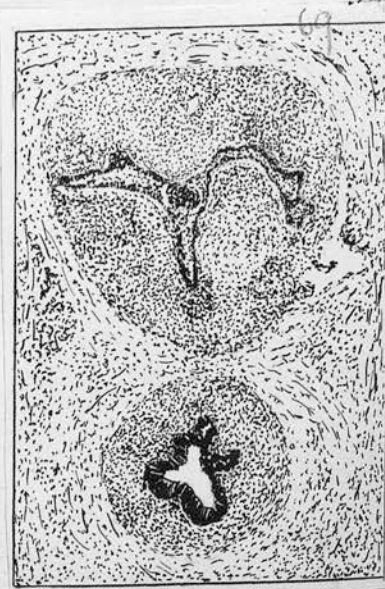


Fig. 69.

Figs. 67, 68 and 69. 110 mm. embryo x 45 -
 (67) = utero-vaginal canal (level i. Fig. 70), (68) = utero-vaginal
 canal (level ii Fig. 70), (69) = (Level iii. Fig. 70)

110 Tube. Fimbriae are now present at the abdominal ostium of the tube. These are not yet very complicated or fine. The interior of the tube exhibits here very defined folds, usually four in number. These have a well-marked supporting mesodermic core, and on their inner surface development of secondary or subsidiary folds is commencing. The lining epithelium is of the tall columnar type, and I cannot detect the presence of cilia. The tubal wall shows an inner longitudinal and outer circular layer of cells. Traced medially its cavity diminishes in size, the folds of lining epithelium becoming lower and less complex, until finally the tube comes to possess a small rounded lumen with a smooth mucous lining (see Figs. 63, 64, 65 and 66).

Uterus and Cervix. The two tubes fuse in the middle to form a single structure with a transversely placed slit-like cavity - the utero-vaginal canal. This is surrounded by a well marked mesodermic condensation derived from, and continuous with, that forming the tube wall.

The round ligaments are well marked, but appear to take origin from the uterine ends of the Müllerian tubes rather than the anterior uterine wall proper, showing that full development of the muscular wall of the uterus to include the inner ends of the Fallopian tubes has not yet taken place, the uterine fundus in consequence remaining bicornuate (see later development



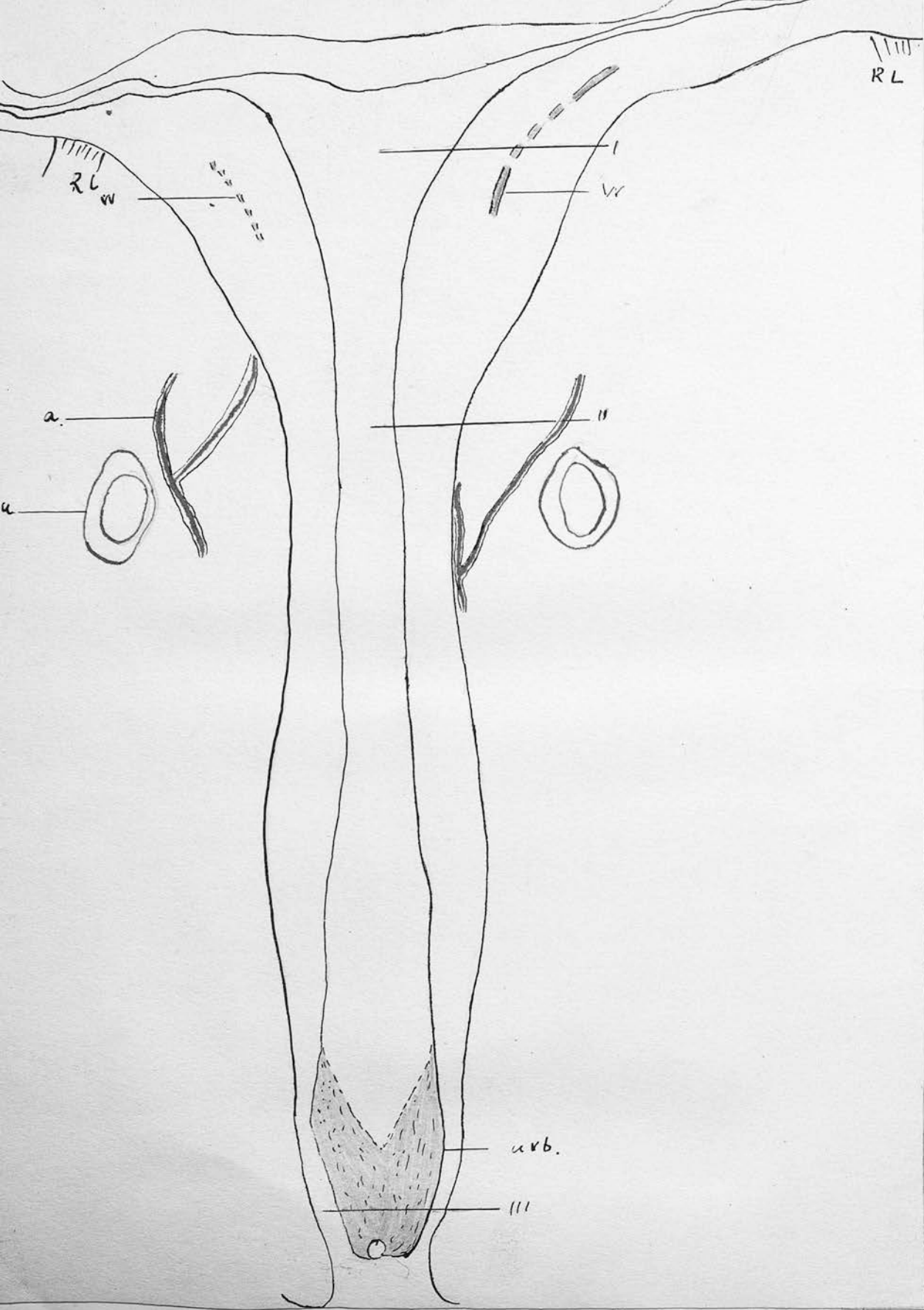


Fig. 70. 110 mm. embryo x 30. Reconstruction of utero-vaginal canal, seen from the front (W) = Wolffian duct, (a) = uterine artery, (u) = uterine vein, (u.v.b.) = utero-vaginal bud, (RL) = round ligament.

of muscular wall of uterus). In this specimen the uterus has a triangular outline and is bicornuate, the fundus is as yet poorly developed and flattened (see Fig.70).

The uterine cavity is lined by high columnar epithelium arranged in low longitudinal grooves on the anterior wall and vice versa. There is no attempt at gland formation (see Fig. 67 and level i. Fig.70).

The walls - mesodermic - are thick and show an irregular arrangement in three cell layers - an inner longitudinal and intermediate retiform, and an outer circular. All three layers show a well marked capillary network of blood vessels, which are most numerous in the retiform layer.

A short segment of Wolffian duct is seen lying on the left side of the uterine cavity, outside the mesodermic condensation surrounding it.

Followed caudally the utero-vaginal canal narrows. Lateral to the mesoderm i.e. wall, the uterine artery ascends sending transverse branches into it.

The epithelium lining the canal becomes taller. The wavy outline of the interior is maintained for some distance, the cavity assuming a S-shaped form, and then gradually giving place to a transversely placed slit-like cavity.(see Fig. 68 and level ii Fig. 70).

A very long narrow cervical canal is present which, before its reduction to a solid epithelial bar by the process of hypertrophy etc. described in the former specimen, widens slightly. From the centre of this epithelial rod, an anterior process grows out of the

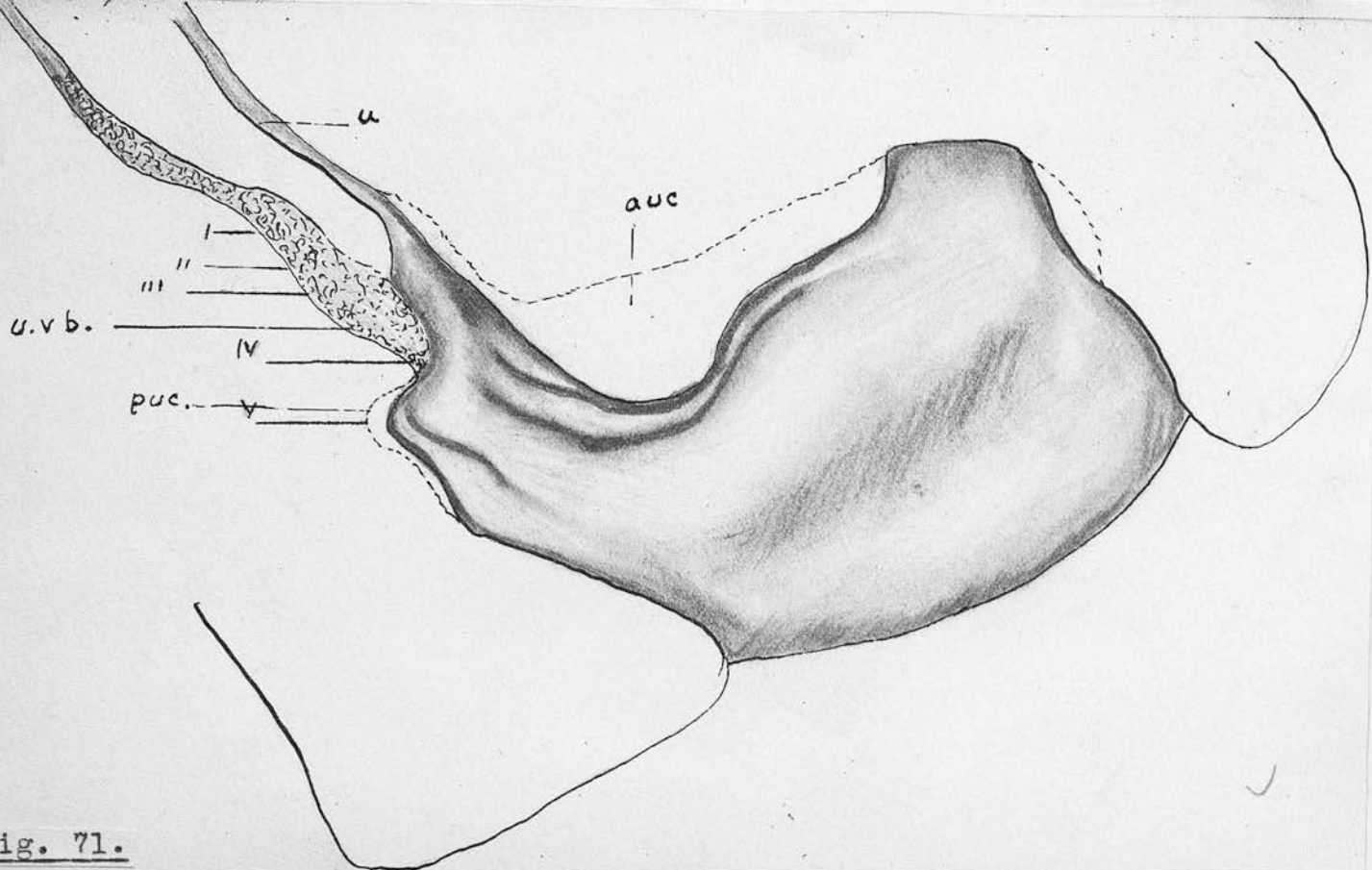


Fig. 71.

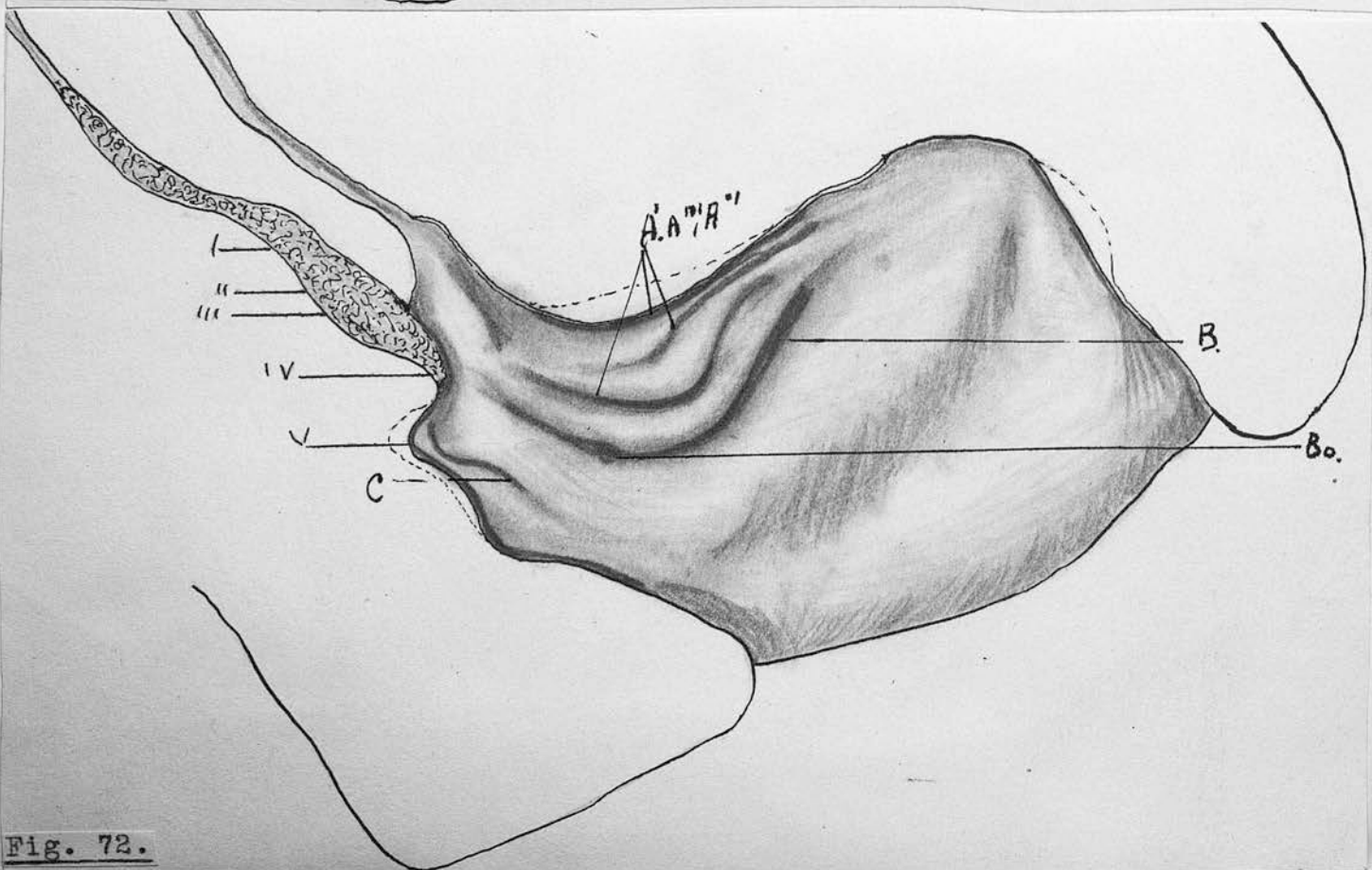


Fig. 72.

Figs. 71, 72 and 73. 110 mm. embryo x 30, (71) and (72) = Reconstruction of sinus seen from the side, (72) after removal of ant. urogenital crest. (73) = transverse sections at levels i, ii, iii, iv, v. Figs. 71 and 72. (u) = urethra, (u.v.b.) = utero-vaginal bud, (a.u.c.) = ant. urogenital crest, (p.u.c.) = post. urogenital crest, (B) Bartholin's groove, (B.o.) = brifice of Bartholin's duct, (C) = groove "C" Aⁱ, Aⁱⁱ, Aⁱⁱⁱ = grooves "A."

cells while, at a slightly lower level, by activity at its lateral angles, two lateral bulbs, in addition to the anterior vaginal bulb are formed (see Fig. 69 and level iii. Fig. 70).

These bulbs in this specimen present great proportions, and a more complicated appearance than in former specimens, without yet attaining that exaggeration of growth that marks the later stages.

As in earlier specimens, the epithelial proliferation is associated with the triradiate shape of the mass on section. The anterior bulb reaches and establishes contact with the upper and posterior part of the sinus wall. There is no evidence in favour of any hypothetical intervention of the Wolffian duct or bulb associated with it.

Sinus 110. (see Figs. 71, 72 and 73). Contact between the utero-vaginal canal and sinus takes place through the agency of the anterior epithelial process as described above. This "bulb" invaginates slightly the posterior sinus wall, and from it, an epithelial downgrowth extends caudally increasing the area of epithelial contact (see levels i, ii, iii, Figs. 71, 72 and 73). The pars phallica of the sinus here is much deepened from above downwards, while the pars pelvina has become shorter and wider. With this change is associated the approximation of the orifice of Bartholin's duct to the utero-vaginal area of contact - the whole being the result of a process of invagination of the posterior sinus wall which is

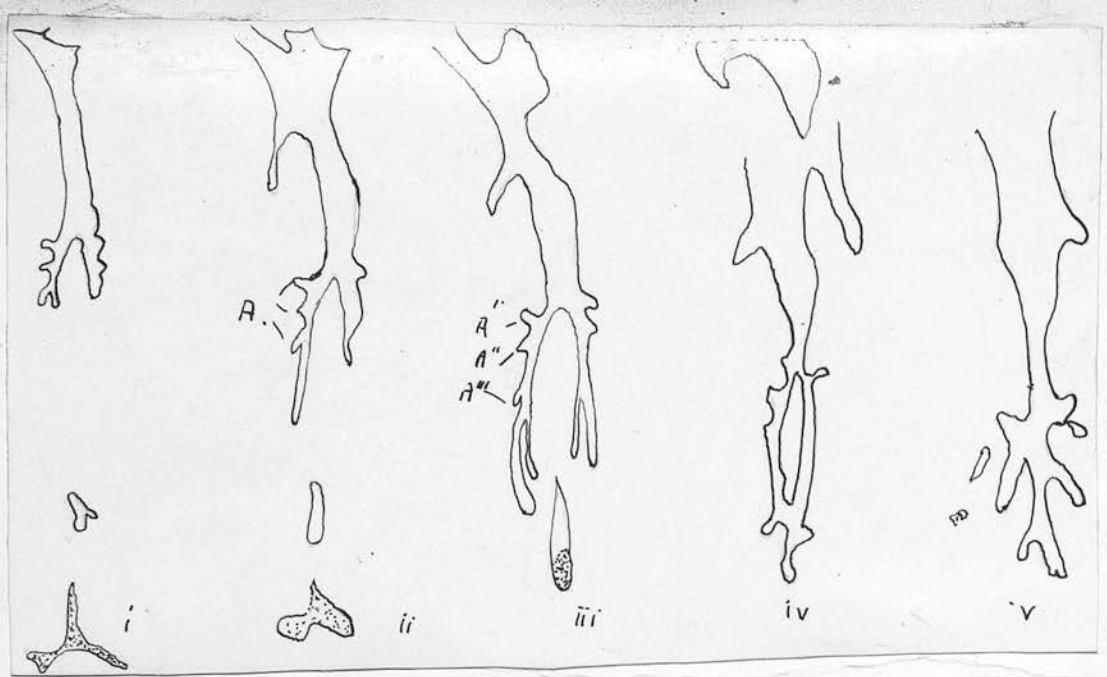


Fig. 73.

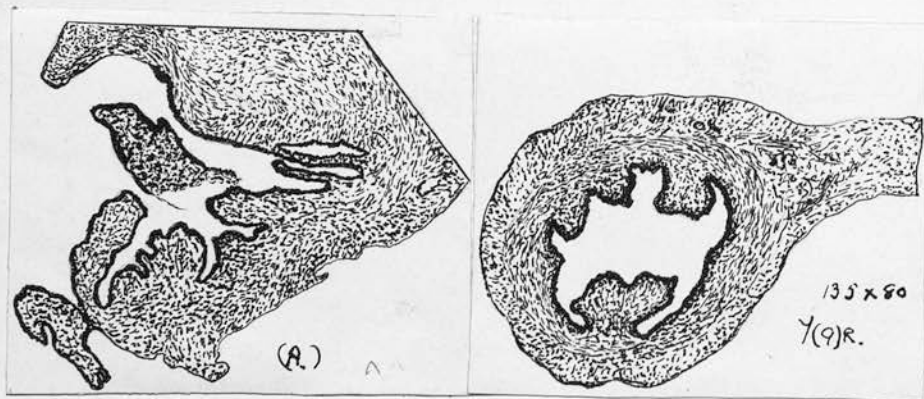


Fig. 74. 135 mm. embryo x 80. Fallopian tube (A) abdominal osti

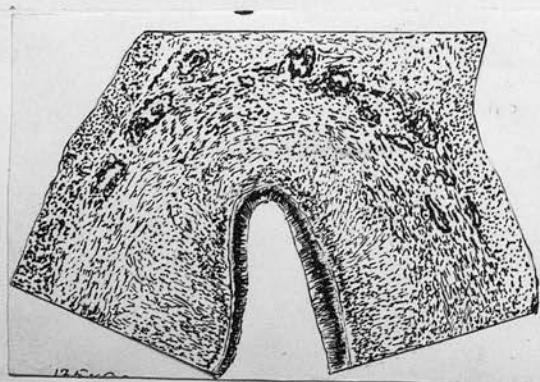


Fig. 75. 135 mm. embryo x 80. Utero-vaginal cavity - proximal par

advancing, *pari passu*, with the growth of the vaginal bulbs. This change will be considered in more detail later.

The anterior Urogenital crest is present - poorly developed in the *pars pelvina*, but forming in the lower part of the latter, and in the *pars phallica*, a deep keel-like downgrowth into the sinus. At the same time that part of the lateral sinus wall which lies under cover of this crest, shows a great increase in complexity.

The original longitudinal groove (A) is now represented by three more or less parallel and horizontal grooves. (Aiii), (ii) and (i) from above downwards - all lying under cover of the anterior urogenital crest and the first in addition being covered by a secondary or subsidiary fold of mucous membrane. (see level iv. Figs. 71, 72 and 73. Bartholin's groove, which is deep and well marked, lies ventral and below the level of this, and is not therefore overhung to any extent by this crest (see level v. Figs. 71, 72 and 73).

Posteriorly the sinus exhibits a small posterior urogenital recess, with a longitudinal groove (C) in its lateral wall. Both labia majora and minora are well developed, but the subclitoridean recess is small and shallow.

The relations and appearances of relief of the sinus wall can be most readily appreciated by comparison of the series of drawings opposite, representing transverse sections of the sinus at various levels, with the lateral reconstruction of the sinus and its surroundings.

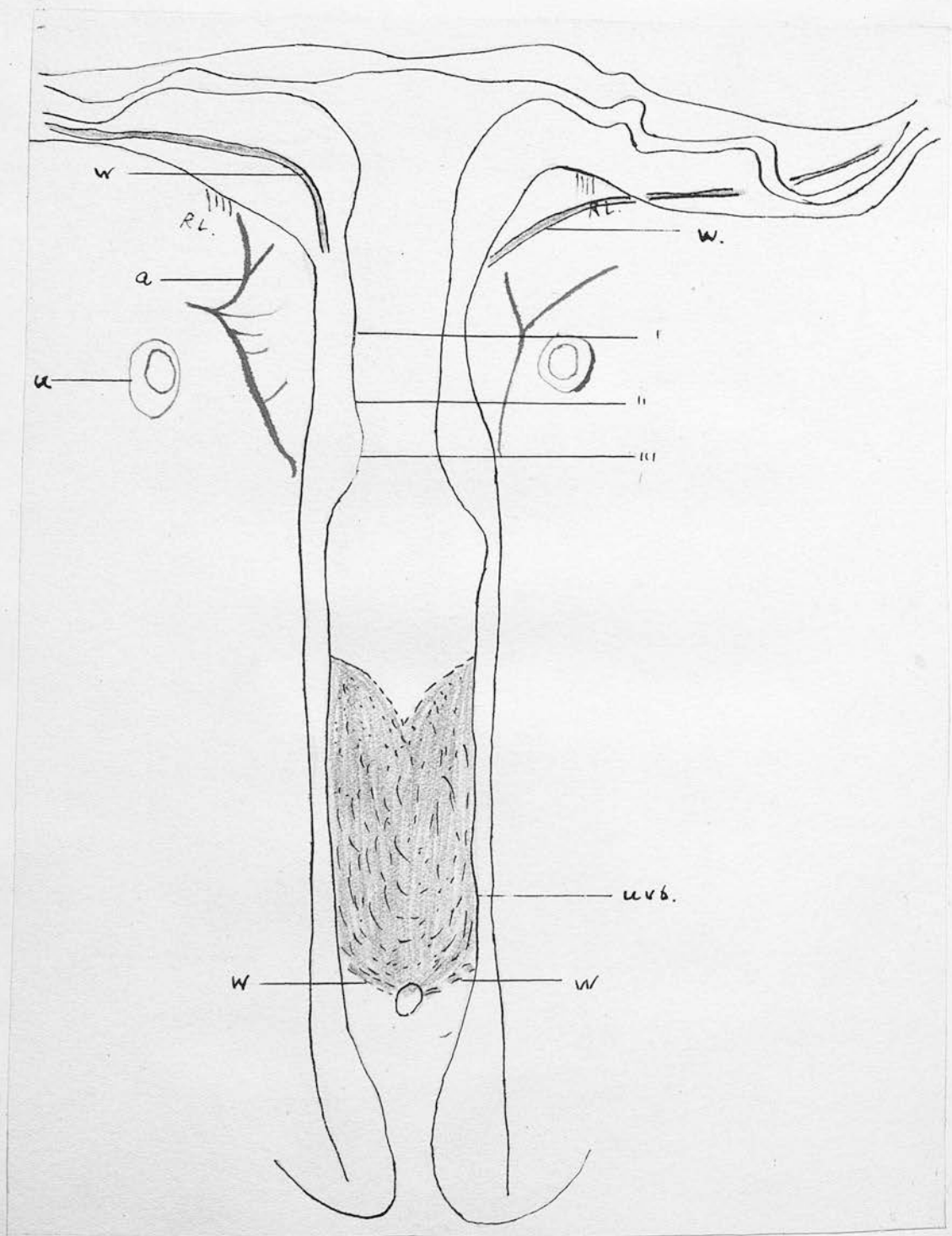


Fig. 76. 135 mm. embryo x 15. Reconstruction of utero-vaginal cavity seen from the front. (W) = Wolffian duct (a) = uterine artery (u) = ureter, (u.v.b.) = utero-vaginal bud. (RL) = round ligament.

135 mm. Embryo.

Tube. The fimbriae at the abdominal ostium of the tube are now very well marked, but still very coarse. The tubal folds now possess secondary ramifications and receive a mesodermic core which appears to be derived from the inner circular cell-layer (see Fig. 74). The tube wall now exhibits an inner and outer circular, and intermediate longitudinal layer. The lumen diminishes in size and loses its folds as it is traced medially.

Utero-vaginal cavity. (Upper or uterine portion) mucous membrane is of the tall columnar epithelial variety, shallow grooves and low ridges are present, but no evidence of gland formation. The cellular nuclei do not stain deeply, but the basement membrane is well marked. The wall shows, externally to the mucous membrane, a layer of cells arranged radially, next to this a very vascular retiform layer and outermost, a well marked circularly arranged layer (see Fig. 75).

In its general shape the fundus is flattened or very slightly concave and the round ligaments still have their origin some little way from the uterine body i.e. in the inner ends of tubes (see Fig. 76).

Wolffian duct. In the parametrium on the right of the uterus a segment of Wolffian duct can be seen. Here this duct possesses a wide lumen, lined by columnar epithelium cells with darkly staining nuclei. A cellular condensation surrounds it, but the definite circular layer found in former specimens is absent. The duct is lost sight

of at a lower level.

Followed caudally, the utero-vaginal lumen at first becomes narrowed and rounded, the internal undulations persisting. A very definite anterior longitudinal groove with two lateral ridges is present.

Note. It is difficult to make out the configuration of the posterior wall as the specimen here is much torn.

These folds now are much more definite than the rather vague undulations present in former specimens, and the mesoderm underlying the mucosa takes part in their formation. They persist as the utero-vaginal canal is followed caudally, and, when the canal again widens laterally, a very interesting internal configuration is present. A prominent anterior crest can be seen opposed to which, on the posterior walls are subsidiary longitudinal ridges and grooves with small secondary depressions. These possibly are gland depressions or the anlagen of the arbor vitae of the cervical canal.

Note. A wax cast reconstruction of the inner aspect of the canal at this site does not show and special and definite relief formation.

The relief of the lumen of the utero-vaginal canal continues to alter as we follow it caudally (i) the prominent anterior groove disappears and is replaced by a low convexity with three small ridges, which correspond with three small grooves on the concave posterior wall, (ii) a canal showing walls with irregular grooves and ridges, which in time gives place to a (iii) comparatively smooth transverse slit-like cavity (see Fig. 77).

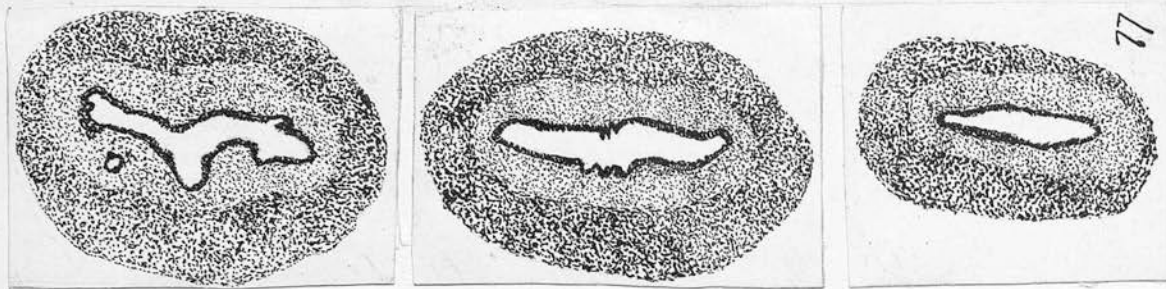


Fig. 77. 135 mm. embryo x 30. Transverse sections of utero-vaginal canal (levels i, ii, iii, Fig. 76.)

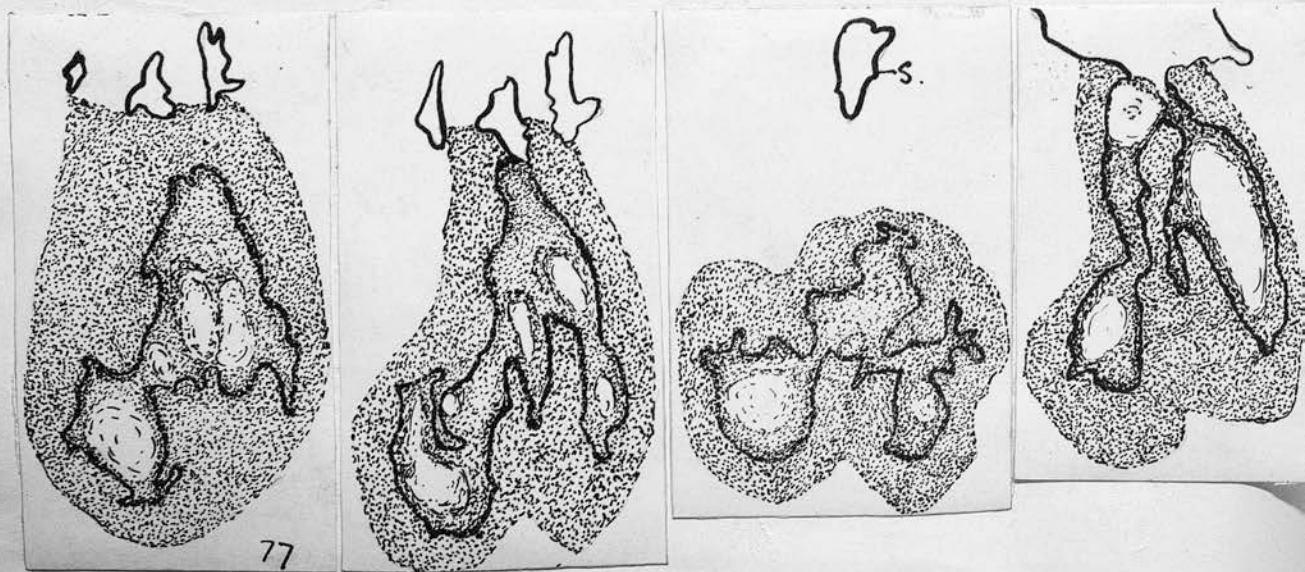
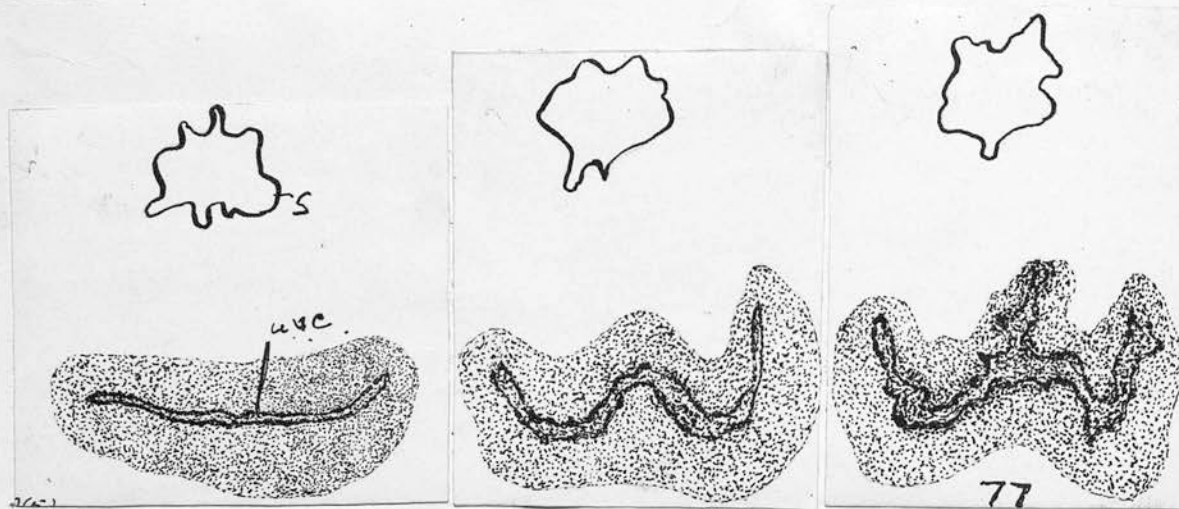


Fig. 78. 135 mm. embryo x 30. Transverse sections of lower end of utero-vaginal canal to show formation of vaginal bulbs (S) - sinus (u.v.c.) - utero-vaginal canal.

This by a process of approximation and epithelial hypertrophy - as before described - commencing at the lateral angles, and proceeding medially, reduces the former utero-vaginal canal to a transversely placed solid bar of epithelium. The cells now filling the lumen are large and rounded, and their nuclei take the stain only lightly. As the bar is followed caudally, the activity of growth of these cells becomes mainly concentrated at three centres - a single median and two lateral, and the three vaginal bulbs so formed project into the surrounding mesoderm as rounded masses possessing vacuolating centres. In addition to these three main centres of activity, the epithelial mass sends out numerous smaller epithelial "knobs", both anteriorly and posteriorly, which later, through disintegration of their contained epithelium, may give rise to the vaginal rugae.

The anterior or median bulb comes into contact with the posterior sinus wall, invaginating it slightly and thus producing a low projection of vaginal epithelium, covered by the lining cells of the sinus. At the apex of this projection the cells are breaking down, allowing communication between the sinus and the cavity which is appearing within the bulbs as the result of the disintegration of their central cells. This marks the site of the hymeneal orifice - limited for the moment of course in extent - while the area of contact of the vaginal and sinus cells forms the upper and central part of the hymen, just below and behind the urethral

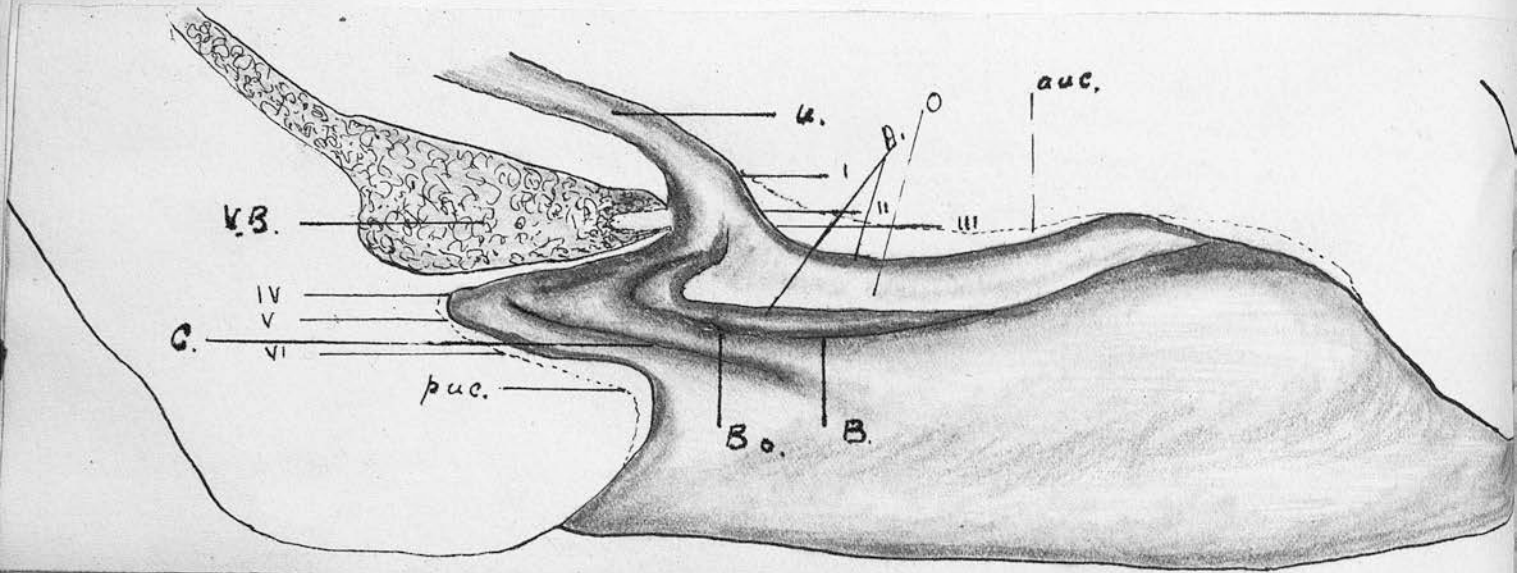


Fig. 79.

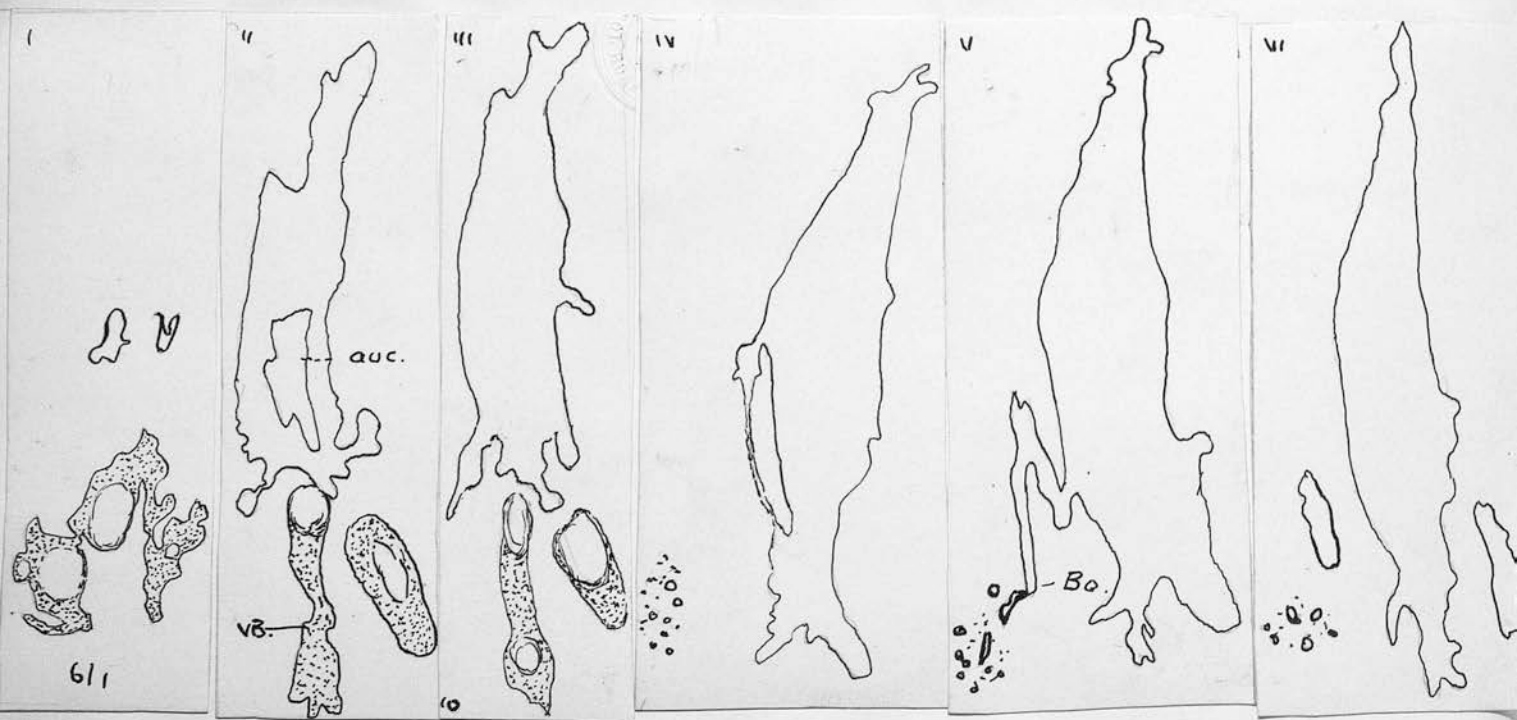


Fig. 80.

Figs. 79 and 80. 135 mm. embryo x 20. (79) = reconstruction of sinus seen from the side, (80) = transverse sections at (levels i, ii, iii, iv, v, vi, Fig. (79.)), (V.B.) = vaginal bulb, (u) = urethra, (a.u.c.) = ant. urogenital crest, (p.u.c.) = post urogenital crest, (B) = Bartholin's groove, (B.o.) = orifice of Bartholin's duct, (C) = groove "C." A. Aⁱ = grooves "A" with "o" = operculum-like mucous flap.

orifice (see Fig. 78).

Sinus 135mm. (see Figs. 79 and 80). By the projection of the vaginal bulb into the posterior sinus wall mentioned above, true invagination takes place. This process which is much more marked now than previously, and which later becomes even more exaggerated, will receive full attention later (see levels i, ii, iii. Figs. 79 and 80).

Also, associated with the inturning of the upper and posterior part of the sinus, the most cephalic part of Bartholin's groove is turned to run almost horizontally and parallel in direction to the utero-vaginal-urogenital area of contact, that is at right angles to the long axis of the sinus. The groove is angled, the lower portion forming a deep depression in the lateral wall of the sinus. It is overhung by a operculum-like flap of mucous membrane and into its depth Bartholin's duct opens (see levels iv, v. Figs. 79 and 80.)

The pars pelvina of the sinus has now, by a process of invagination, almost disappeared, while the pars phallica is shallow from above downwards, and much lengthened in its antero-posterior axis.

The anterior urogenital crest is low and poorly marked. A small posterior urogenital recess is present, the epithelial indentations before mentioned (of doubtful significance) being well marked in this specimen (see level vi. Figs 79 and 80).

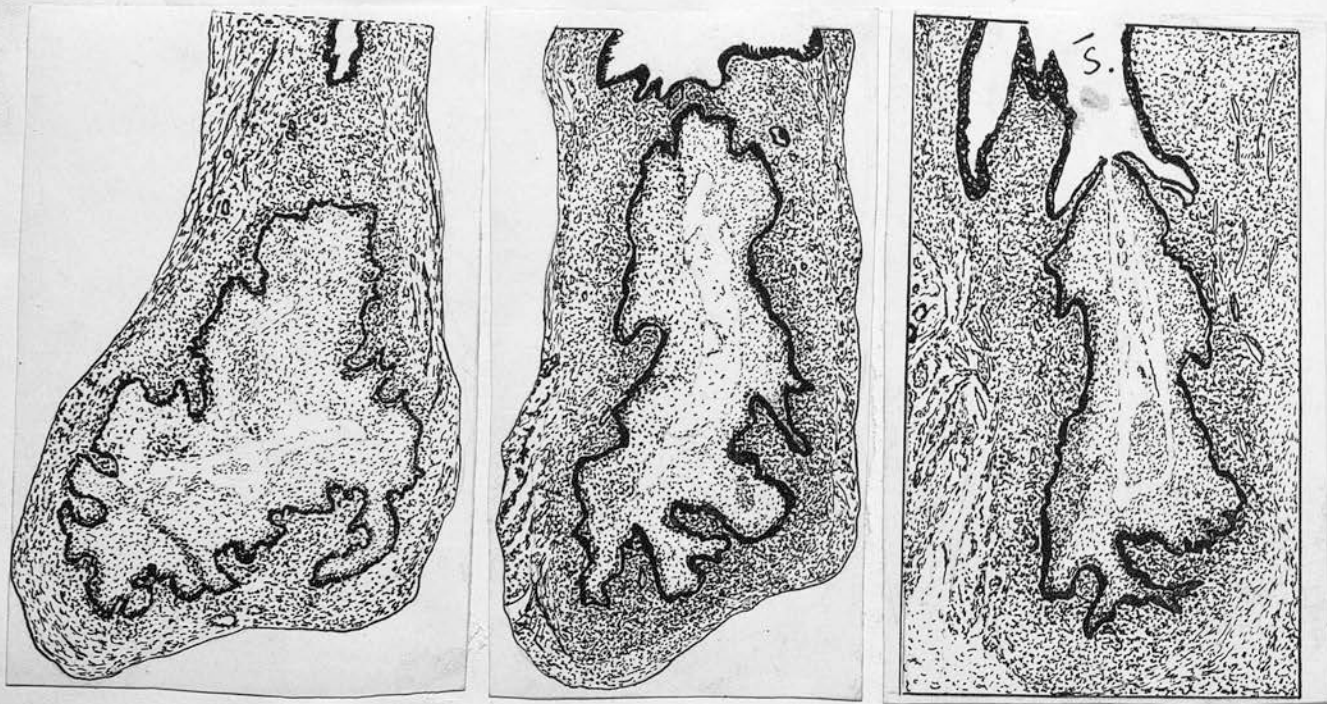
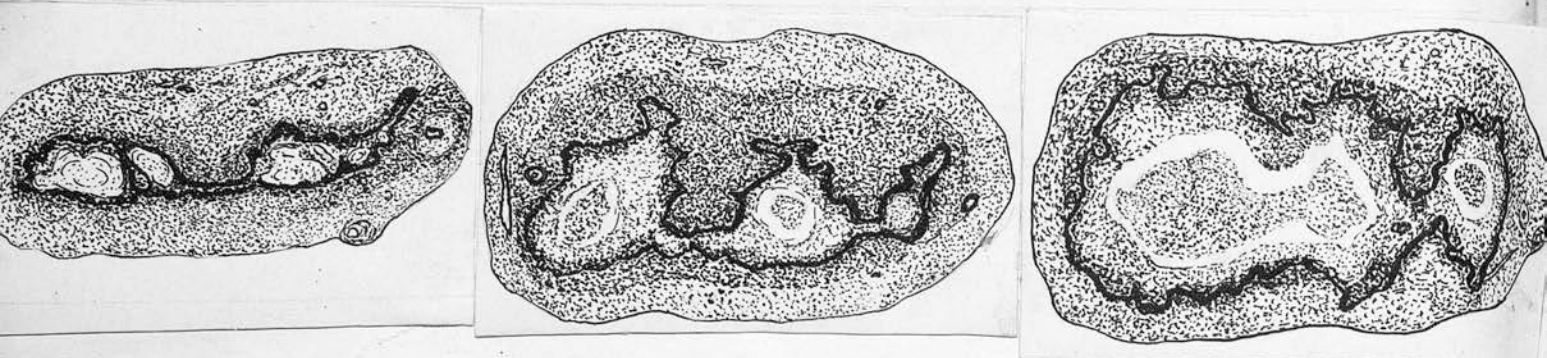


Fig. 81. 170 mm. embryo x 20. Transverse sections through distal part of utero-vaginal canal to show further development of vaginal bulbs. (S) = sinus.

165-170mm Embryo.

The upper part of the genital canal is not included in this specimen, and I shall therefore commence the description at about the level of the lower part of the cervical or upper part of the vaginal canal.

When first seen the utero-vaginal canal is represented by a solid bar or crescent of cells, its concavity directed forward, and its contours of rather wavy outline. The Wolffian duct is seen lying in the vascular mesodermic condensation surrounding the utero-vaginal canal, and postero-lateral to this structure. The cells surrounding the duct are arranged circularly, but elsewhere the arrangement of the mesoderm is quite irregular.

As development proceeds, the vaginal epithelial mass increases in size, antero-posteriorly rather than laterally, this increased growth of activity taking place mainly at certain centres or bulbs. These, in the present specimen, are not so definitely three in number as in former specimens, but the whole area tends to assume the triradiate shape before described, the "bulbs" gradually giving place to the formation of a large irregular epithelial mass which extends forwards and downwards towards the posterior sinus wall. This large bulbous lower end of the vagina reaches and markedly invaginates the posterior sinus wall, leading to a somewhat cone-shaped projection into this cavity. This receives a covering of the lining cells of the sinus on its sur-

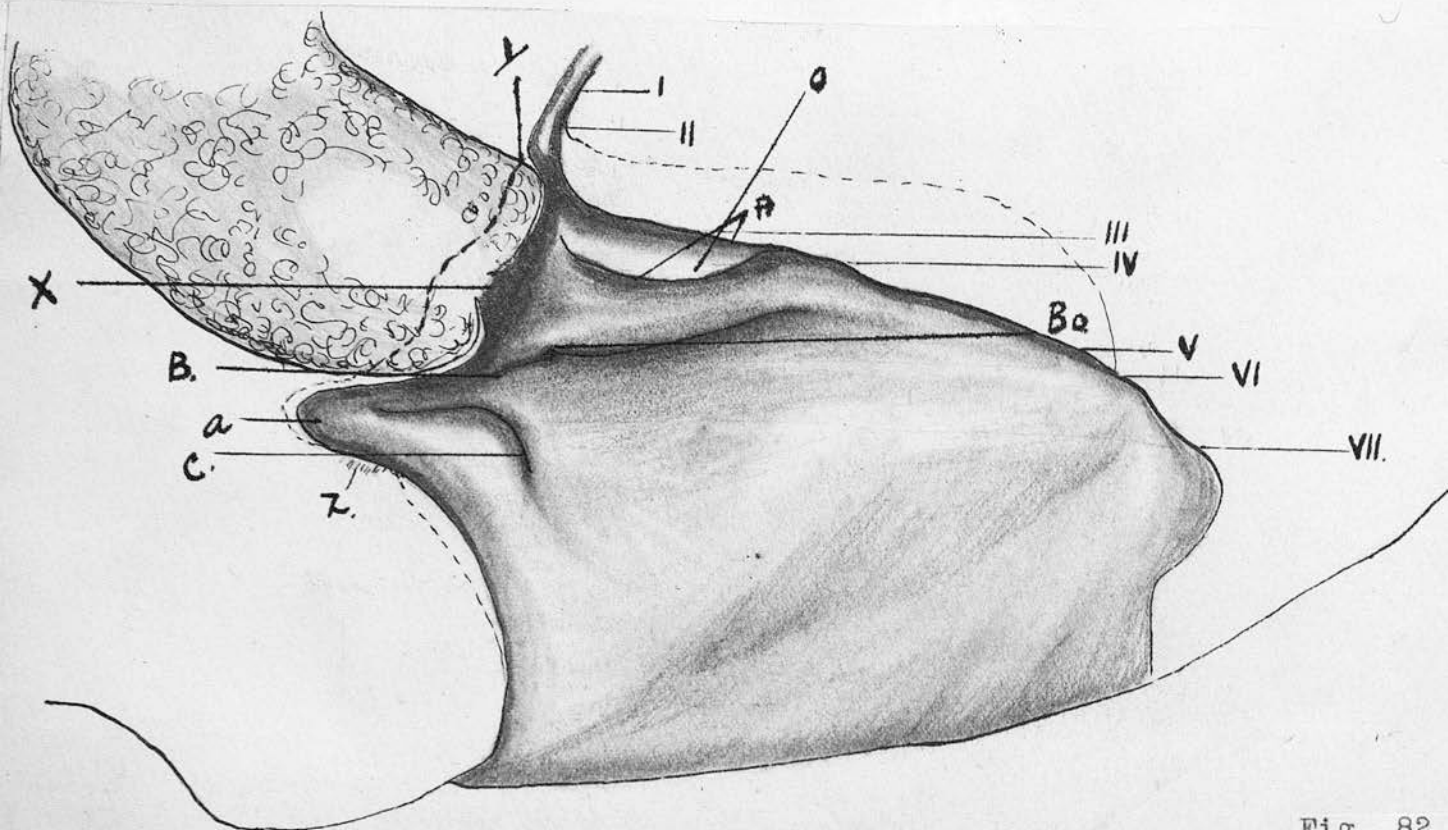


Fig. 82

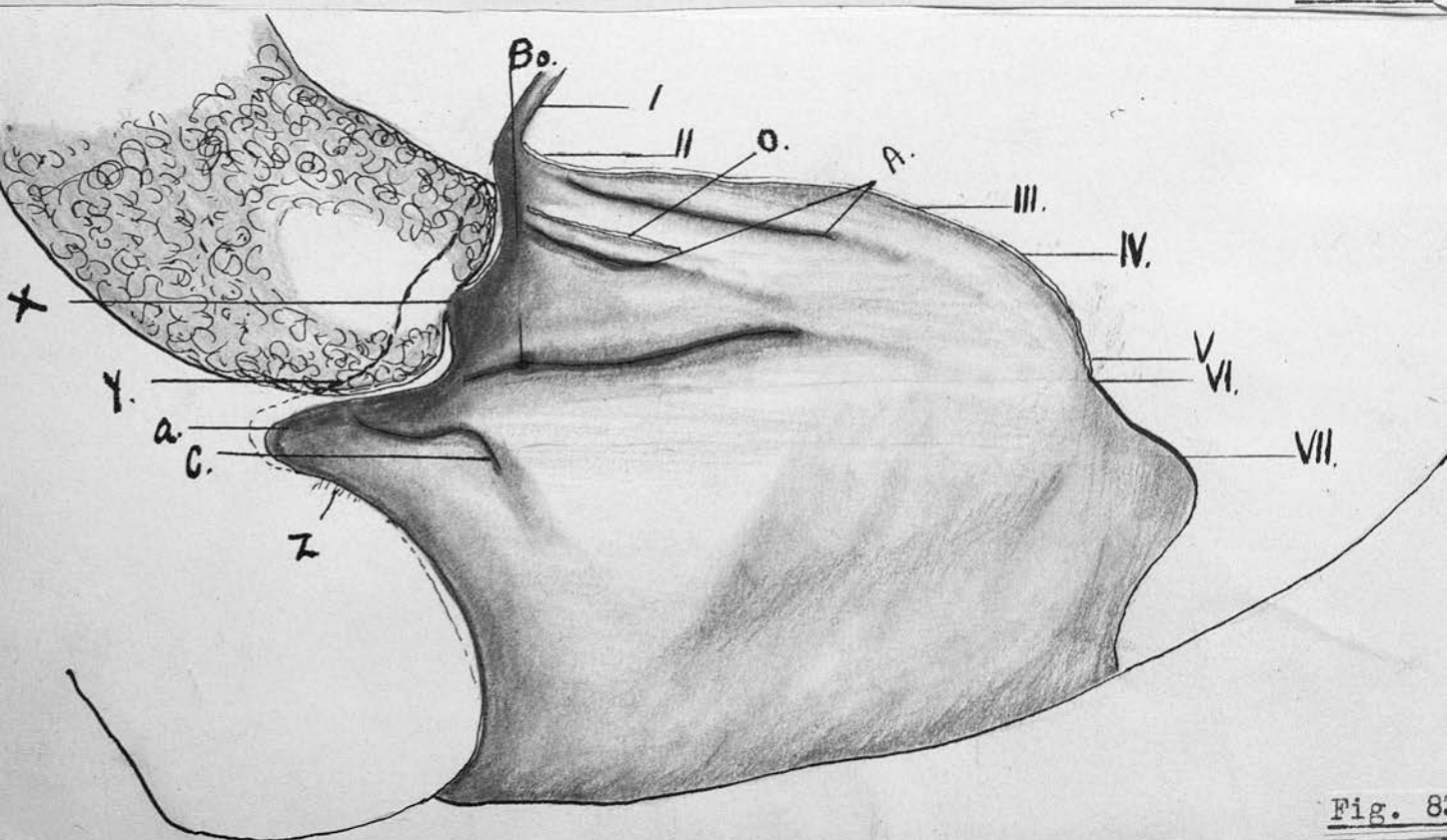


Fig. 83

Figs. 82, 83 and 84. 170 mm. embryo x 20 (82) and (83) = reconstruction of sinus seen from the side, (83) after removal of ant. urogenital crest, (84) = Transverse sections through levels i, ii, iii, iv, vi, vii, Figs. (82) and (83). (B.) = Bartholin's groove, (B.o.) = orifice of Bartholin's duct, (C) = groove "C" (A) = grooves "A" (O) = opening of culum like flap (cut off in fig. 83), (a) = subbulbar recess. Z. = site of epithelial indentations.

face. The central cells of the vagina are breaking down, and the cavity so formed communicates with that of the sinus at the apex of the projection, so marking the site of the hymeneal opening (see Fig. 81).

The basic structure of the hymen can therefore be seen in this specimen. It is seen to consist of cells derived from the vaginal mesoderm, covered superficially by sinus epithelium and possesses an intervening layer of vascular mesoderm derived from the condensation round the walls of the cavities.

Sinus 165-170mm. (see Figs. 82, 83 and 84). The lateral wall of the sinus in this specimen has undergone a very great increase in the complicity of its relief. We have seen how the great bulbous growth invaginates the posterior-superior sinus wall, breaking through this at the apex of the projection so-formed, to allow communication between the sinus cavity and that formed by the vacuolation and breaking down of the central cells of the vaginal bulbs, to form the future hymeneal opening - marked "X" (see Figs. 82 and 83).

By the invagination of the posterior sinus wall, a deep groove or depression is formed, represented in the diagram by the dotted line Y. Shortly distal to this, and lying roughly parallel with it, is Bartholin's groove (B), into the depth of which opens Bartholin's duct. The marked invagination of the sinus can best be appreciated by comparing the distance of this point B (the opening of Bartholin's duct) from the hymeneal

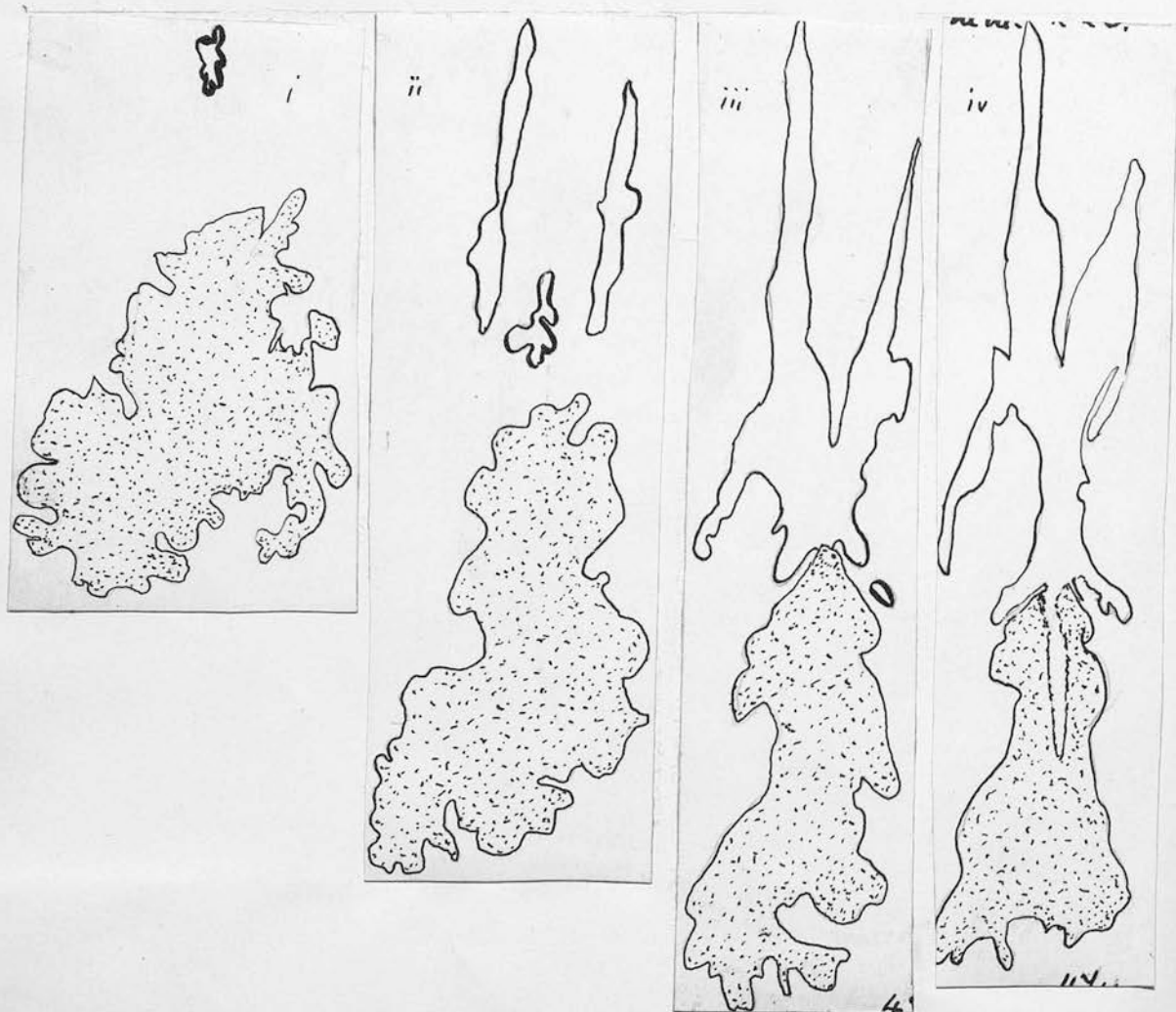


Fig. 84

opening (X) = X B with that in earlier specimens
= X B + Y x.

Thus the distance from B Y plus that from Y to the crest of the hymeneal prominence "X", is the distance between the Bartholin site and the posterior wall of the sinus, of the earlier stages (i.e. YB+YX) modified now by progressive infolding.

Not only does the vaginal bulb press against the posterior sinus wall, but it also grows along behind it, thus enormously increasing its area of contact with the sinus, and by its "pressure of growth" forcing some of its cells up i.e. cephalically, a little way towards the urethral orifice.

As stated above, the relief of the lateral sinus wall has greatly increased in complicity, certain folds and recesses remaining constant, but exaggerated, while others appear, probably to some extent irregularly and inconstantly.

The anterior urogenital crest is deep and keel-like and under cover of it the fold "A" is seen, much deepened. A second fold "A" lies below parallel to it, under cover of an additional operculum-like flap of mucous membrane (levels ii, iii, iv. Figs. 82, 83 and 84).

The groove "B" - Bartholin's groove - is exaggerated to form a deep epithelium lined recess, into the posterior part of which Bartholin's duct opens (levels v, vi. Figs. 82, 83 and 84).

Below the site of contact of the vaginal bulbs with

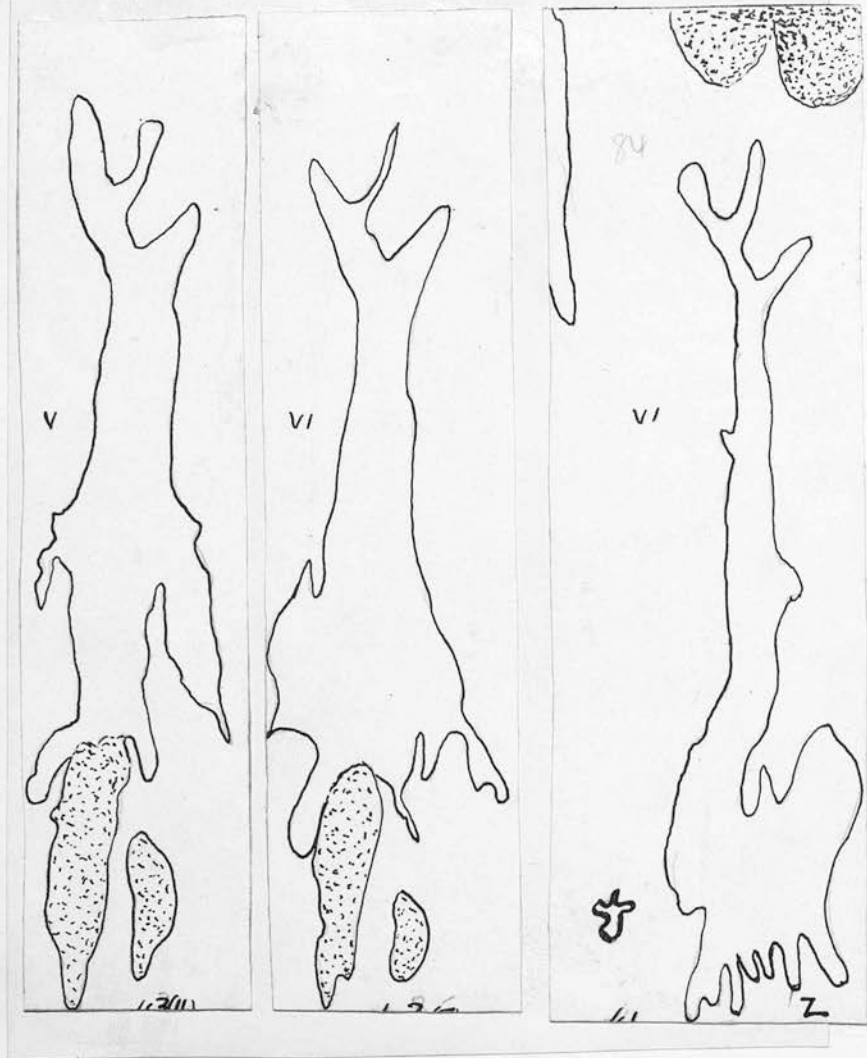


Fig. 84 (contd.)

the posterior sinus wall are certain diverticula or prolongations. These, with the tube-like infoldings of the mucosa, are associated with the invagination of the sinus and one in particular forms a definite "subbulbar" recess. (A smaller recess, which I have called the posterior urogenital recess, has been described in earlier specimens). Lying parallel to the mouth of this recess is the groove "C", shallow in former specimens but here deepened to form a well marked recess. (level vii. Figs. 82, 83 and 84).

The epithelial diverticula mentioned above, were noticed by Mijsberg (27) who looked on them as active outgrowths. This was, to some extent, also our view so far as their extremities were concerned, but we have the impression that in their greater part they are probably only side effects of the invagination.

The Vaginal Bulb. Invagination of the Sinus and formation of the Hymen.

In describing the above specimen, the vaginal bulbs and their development have been repeatedly mentioned without any very detailed account of the structure being given. At the same time the invagination of the posterior sinus wall associated with their development has received only cursory attention. As these changes and structures are closely associated with the formation of the lower end of the vagina and of the hymen, their description must now receive detailed study.

We have seen that, as early as the 65-79mm stage, the distal portion of the fused Müllerian ducts shows activity of its epithelium which tends to be concentrated

at three main centres or bulbs. These as described previously, are placed two laterally, and one centrally, the latter projecting anteriorly in a keel-like fashion, making contact with the posterior sinus wall.

The formation of the vaginal bulbs progresses steadily, and, by 110 stage, these are well formed structures. After this period there is a progressive actual and relative increase in size of the lower end of the utero-vaginal canal. The general nature of this growth has already been indicated, but may with advantage be repeated here with some additional details. Just above its lower end the lumen of the canal is occluded as the result of the activity of its lining cells. As it is followed down, this activity is seen to become concentrated mainly in three "centres", a single median and two lateral, and the three "vaginal bulbs" formed in this way project into the surrounding mesoderm as rounded masses possessing vacuolated centres. The anterior or median bulb is in contact with the posterior sinus wall, invaginating it slightly and thus producing a low projection of vaginal epithelium covered by the lining cells of the sinus. At the apex of this projection the cells are breaking down, allowing communication between the sinus and the cavity which is appearing within the bulbs as a result of the disintegration of their central cells. This marks the site of the hymeneal orifice - limited for the moment, of course, at this state, while the area of contact of vaginal and sinus cells forms the upper central part of the hymen, just below and behind

the urethral orifice.

That this appearance, becoming more evident and important as development goes on, is the result of a true invagination and infolding of the posterior wall of the sinus, and not merely by a growth of this wall to keep pace with the bulging epithelial vagina, is shown by the altered relation of the hymeneal site to the various grooves on the lateral wall of the sinus.

The configuration of the lateral wall has already been briefly noticed, and one groove in particular - that into the depths of which Bartholin's duct opens - has been pointed out. As development proceeds, the relief of this wall becomes more complicated, with the formation of additional grooves and folds. Certain grooves, however, can be found at all stages, and among these is that just mentioned as receiving the duct of Bartholin's gland. The gland and its duct remain in the same relation to each other, the gland deeply fixed in surrounding structures, and the duct running upwards and forwards from it. The duct aperture can therefore be taken as marking a constant point in the sinus, and affording a definite level from which relative measurements may be made. It will be found that, as growth goes on, the duct opening and hymeneal level get nearer: as the duct is fixed, it follows that the hymeneal level is being brought down, and this implies invagination of the upper part of the sinus.

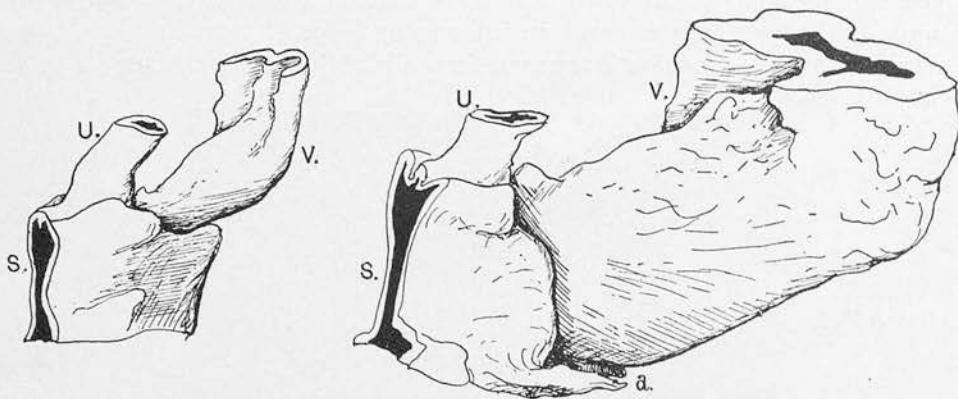


Fig. 10. The lower end of the vagina (V.) at 135 mm. compared with one of 170 mm., showing the relatively enormous growth. Drawn from models made at the same magnification. S., part of the sinus, invaginated above and behind by the vaginal growth; U., urethra. The "outgrowths" from the sinus below the bulbs are indicated at a.

Fig. 85. From the "Development of the Lower End of the Vagina " J.E. Frazer & Alice Bloomfield. p.19.

The additional folds in the wall of the sinus, which appear as development proceeds and seem to be somewhat variable, are probably associated with this inturning of the upper part of the sinus. It is interesting to observe that they appear higher up than the orifice of the duct, and that there is a tendency to the formation of a groove in a transverse plane as growth goes on, just below the level of the hymen, where in fact such a groove might be expected to form with increasing vaginal pressure from behind.

As development proceeds, we find the vaginal bulbs - and, to a lesser extent, the whole vagina - growing at a rate quite out of proportion to the growth of neighbouring structures. This can be shown by comparing the two stages, 135mm and 170mm (see Fig. 85). The reconstructions were made at the same magnification, and the vaginal formations in the older specimen are enormous compared with those in the earlier one: yet the urethrae are little different in size and the differences in the sinus are only in proportion to the general increase, although this point is not very evident in the figure, only a small part of each sinus having been modelled.

This 170mm specimen presents conditions so suggestive and important for the present study, that further consideration of it is pardonable. It has been seen that the very large bulbous end of its vagina has markedly invaginated the posterior wall of the sinus, and this leads to a somewhat cone-shaped projection into this cavity. This receives a covering of the lining cells of the sinus on its surface. The central cells of the vagina are breaking down, and the cavity

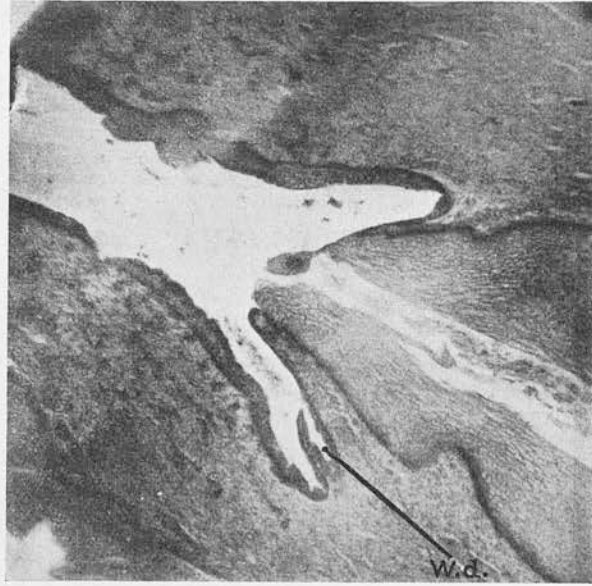


Fig. 12. Section, 170 mm., showing invagination of wall of sinus by vaginal bulbs, with formation of hymen. In the process the lower end of a persistent Wolffian duct, *W.d.*, has been turned in and opens on the hymen. The composition of the hymen is also seen, as well as the cellular conditions within the vagina.

Fig. 86. From the "Development of the Lower End of the Vagina" J.Ernest
Frazer & Alice Bloomfield p.20. Microphotograph

so formed communicates with that of the sinus at the apex of the projection, so marking the site of the hymeneal opening.

One of the most interesting features of this specimen is the presence of a Wolffian duct on one side, which reaches the sinus and extends for a considerable distance upwards beside the vagina. The lumen of this rudiment is small but clear, and is surrounded throughout by a single layer of cubical cells, there being no indication whatever of any cellular activity in the direction of division or hypertrophy; the layer is only a persisting simple lining layer. When followed down, the duct, embedded as in all cases in the lateral part of the thick condensation surrounding the vagina, is found to open on the surface of the hymen a little distance from its "free border" or opening (see Fig. 86). It is evident that the part of the wall of the sinus on which the duct originally opened has been invaginated, or turned in by the growth of the vaginal bulbs behind it, and has thus come to form part of the superficial aspect of the hymen. Lastly, it has to be noted that the Wolffian tube nowhere in its course shows any sign whatever of contact or fusion, past or present, with the vaginal epithelium, nor (as has been pointed out) is there any smallest indication of past or present bulb-formation about it; it is a separate structure, not concerned with the activities in progress in the vagina, and its presence in this case is a happy accident which in its conditions bears out to the

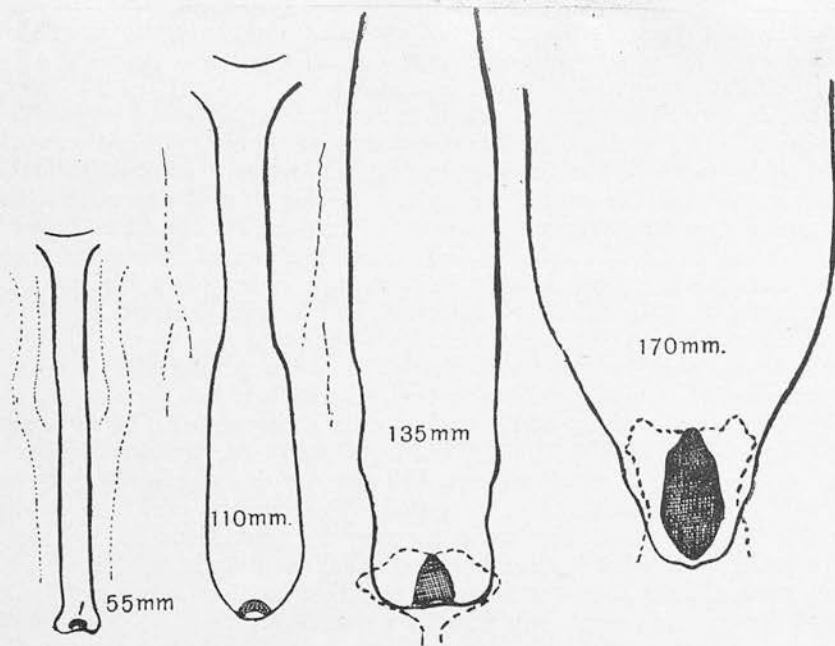


Fig. 13. Schematic reconstructions. The utero-vaginal length is shown in the first two diagrams the vagina only in the third, and its lower portion only in the last. The area of contact with the sinus is shaded, and the outline of the neighbouring part of the sinus given in interrupted lines. Magnification the same in all.

Fig. 87. From the "Development of the Lower End of the Vagina," J. Ernest Frazer & Alice Bloomfield, p.21.

full the inferences drawn from examination of stages in which no rudiment was to be found.

The relatively enormous bulbous growth in this foetus is only the modified representative at the lower end of the vagina of a disproportionate increase in size found in the canal above this. The striking size of the bulbs in Fig. 85 would be lost to a large extent if they were viewed from behind, for there is marked side to side compression. The vagina higher up, on the other hand, is widened laterally to a considerable degree and compressed from before backwards. Fig. 87 represents these relations by schematic reconstructions of four stages: it can be seen that, whereas the increasing vaginal breadth in the first two stages does not markedly exceed a growth proportionate to the general increase, that of the 170mm stage is quite disproportionate.

The bulbs show, centrally, large rounded vacuolated cells staining poorly, which are disintegrating, while the more externally placed cells are small and stain well, and are apparently growing rapidly and pushing their way into or within the surrounding mesoderm. A question arises at once as to the source of these cells, but there does not seem to be any reasonable doubt about the matter. Apart from the fact that this epithelial plug exists at a time when the Wolffian ducts are present and open separately in the sinus, we have seen that in all the subsequent stages mentioned in this paper there has been no evidence or suggestion of any sort of bulb-formation in the Wolffian ducts, when these could be traced, and, a fortiori, no hint of any participation of these ducts in the formation of the vaginal bulbs. The same can be said about the suggestion that the cellular bulbs might be derived from the urogenital sinus: the vaginal structures are solid masses of cells before the blending of the respective epithelia occurs, and in none of our sections of later

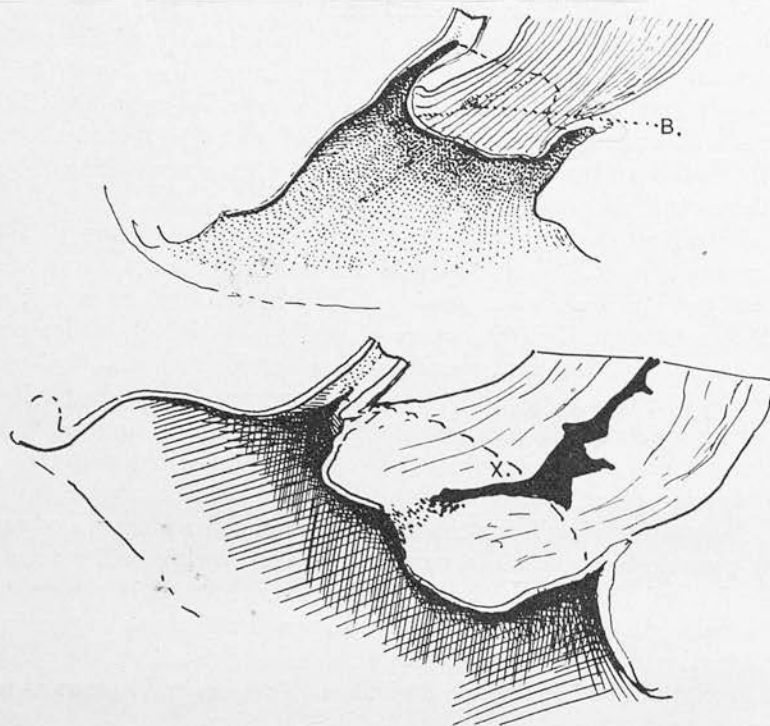


Fig. 14. Sagittal sections of (above) 240 mm. fetus, and (below) fetus at term, at similar magnification. *B.* and *X.* indicate the situations of the openings of the ducts, deep to the hymeneal projection.

Fig. 88. From the "Development of the Lower End of the Vagina," J. Ernest Frazer & Alice Bloomfield, p.23.

stages is there any appearance of ingrowth from the sinus, but rather of vaginal projection into this cavity. The utero-vaginal canal and the Wolffian duct remnants, when present, are surrounded by a condensation of mesoderm which is directly derived or continued from the condensation of the genital stalk. With the appearance of the bulbs, it has to be decided whether their form is the result of a high degree of activity of the vaginal cells, or is due to an invasive action of the surrounding cellular condensation. When we see the relative increase in size of the two contrasted regions, and observe the way in which the condensation layer is moulded on the contained vaginal growth, there seems no reason to doubt that the former is the correct explanation. If the irregular bulbar outline were due to invasion by the surrounding cells, one would not expect such altered shape and accommodation to the bulbar outline, but rather the maintenance of the original regular form.

The method by which the lower end of the vagina is formed and its area of contact with the wall of the sinus is enlarged, as we have described it in this paper, progresses up to birth at least, and the increasing invagination of the upper and back part of the sinus wall causes an increase in size of the hymen and brings it nearer to the surface. Fig. 88 shows the condition in a specimen of 240mm. This last process of invagination has gone on to such an extent that the orifice of the duct of Bartholin's gland is now hidden by the projecting hymen, and is not very far from the base or line of inflection of the hymen: it is interesting to observe, in this foetus, that the upper end of the long groove, into the depths of which the duct opens, reaches and is turned down on the side of the hymen.

The second section shown in Fig. 88 is that of a foetus at full term, in which the orifice of the duct is close to the base of the hymeneal inflection. (In this

connection it is to be noted that the opening of the Wolffian duct on the base of the hymen is probably secondarily acquired, its true developmental position being situated on the free edge of hymeneal).

It shows the final foetal stage of the invaginating process which was initiated some 4-5 months previously.

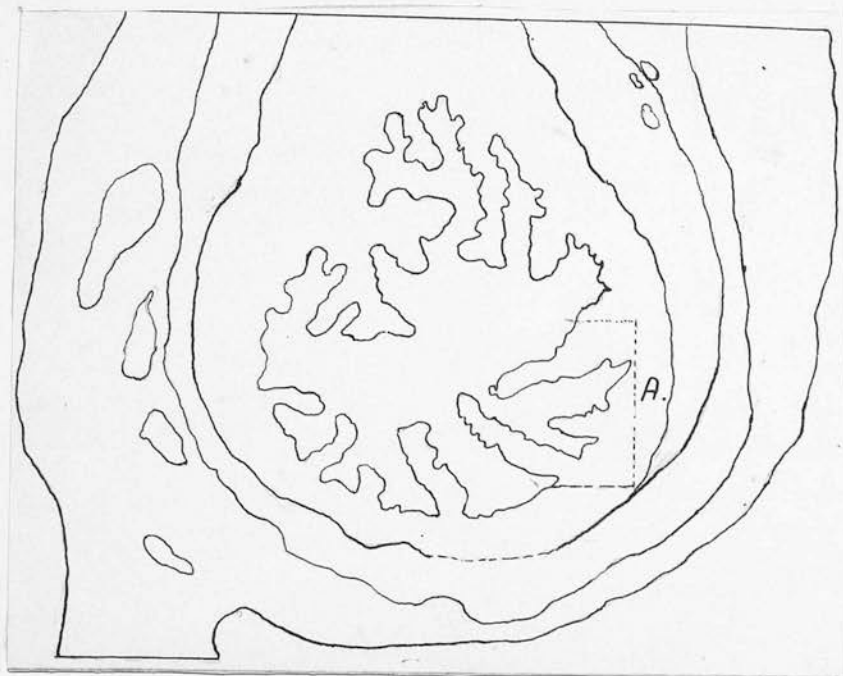


Fig. 89.

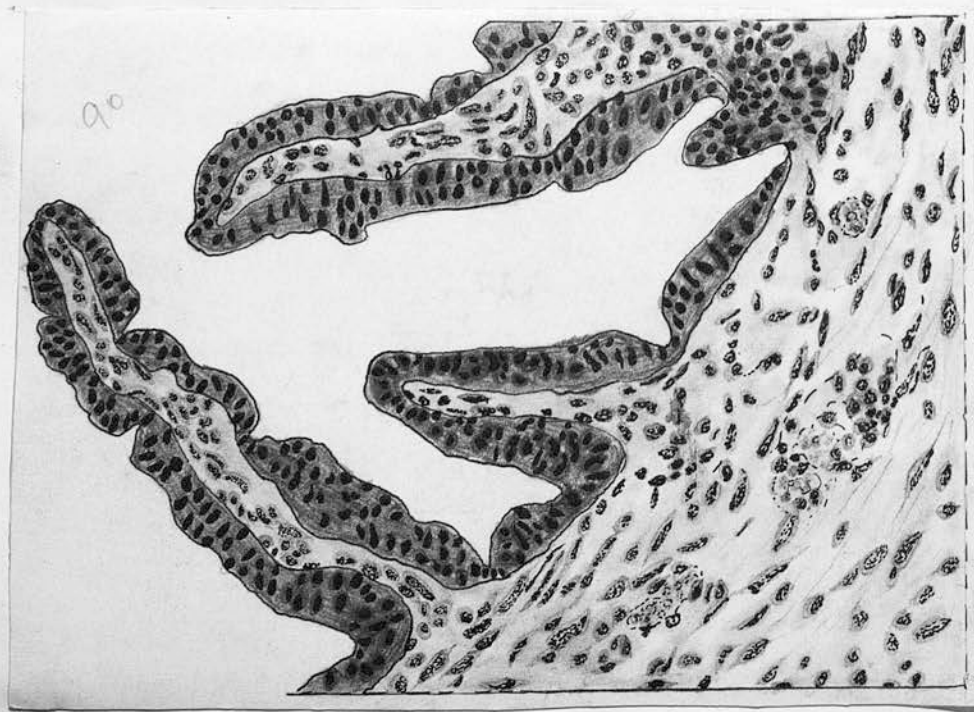


Fig. 90

Figs. 89 and 90. New Born Child, Fig. 89 x 74. Fig. 90 x 320 Fallopian tube. Area A. in Fig. 89 enlarged to show histology in Fig. 90.

SUMMARY OF DEVELOPMENT OF TUBE & UTERUS & VIEWS OF

OTHER WORKERS.

Tube. The development of the tube has now been traced through successive stages, and the following points may be noted.

Mucous Membrane. From the early smooth mucous membrane of the Müllerian Ducts, slight irregular folds in the interior are seen by the 48mm stage, no true fimbriae being present at the abdominal ostium as yet.

By the 79mm stage, regular folds, usually four in number are present in the interior of the outer $\frac{1}{3}$ of the tube, the abdominal ostium possessing irregular margins with occasional blunt finger-like fimbriae.

The tube of the 110 mm specimen shows a more complex interior, but, while the folds are now more numerous and receive a mesodermic supporting frame-work from the tube wall, these are still comparatively blunt and simple, as are the fimbriae at the ostium abdominale.

Through successive stages to the last month of foetal life, the tubal folds increase in number and complexity, the primary folds developing secondary branches into which penetrates a fine vascular mesodermic core. Figs. 89 and 90 show outlines of the lumen of the tube at birth. For comparison I have included a diagram of the lining of the tube at $3\frac{1}{2}$ years and the enormous increase in number, slenderness and complexity of the tubal folds can be appreciated (see Figs. 91 and 92).

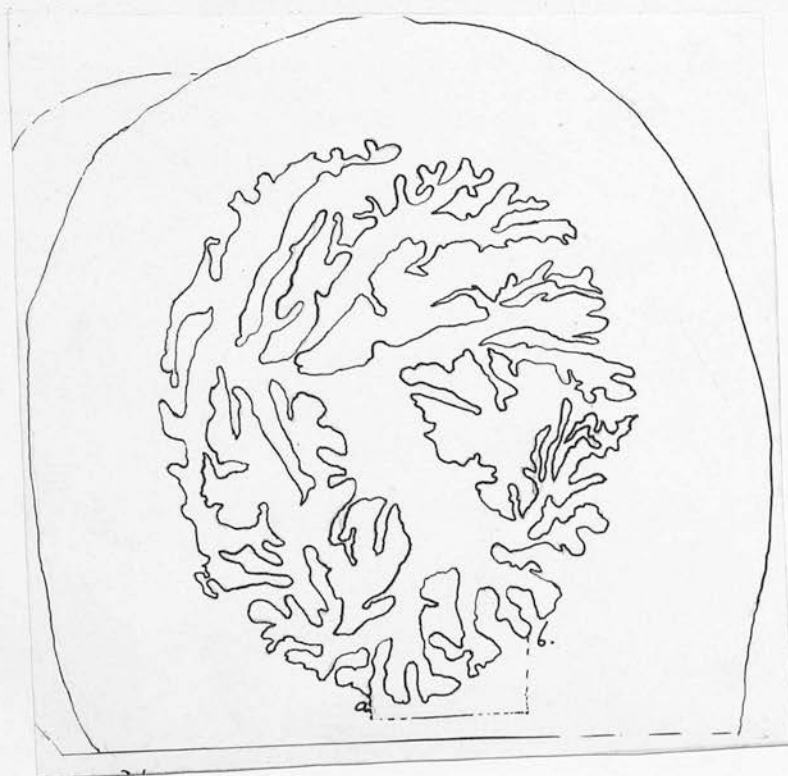


Fig. 91.

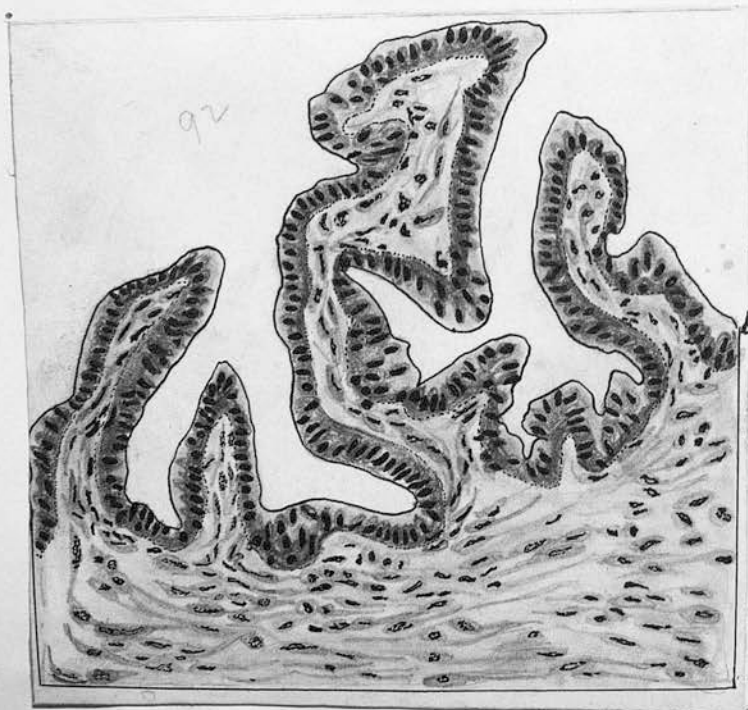


Fig. 92.

Fig. 91 and 92. Child aet $3\frac{1}{2}$ years. Fig. 91 x 74. Fig. 92 x 320. Fallo
tube. Area (a b) Fig. 91 enlarged to show histology in Fig. 92.

The meaning and origin of the complicated folds in the tube wall are difficult to explain.

Wendeler (20) is of the opinion that the active element in their formation is in the mesodermic layer of the tube wall. He describes a marked activity of the sub-epithelial and inner mesodermic layer, by which processes are pushed towards the lumen with a covering of epithelium, tubal folds being thus formed.

Against this, I think, is the fact that, when folds are first noticed in the tube wall, i.e. at the 48mm stage in my series, these consist of the mucous layer only.

On the other hand, the inner mesodermic layer is poorly developed between the fimbriae, opposite which it appears to be growing out to support the epithelial processes, and certainly the cellular vascular mesoderm appears to possess greater potentialities in this direction than does the rather simple columnar epithelial lining which shews no great evidence of growth activity, in the form of heaping up of epithelium etc.

Lawson Tait (28) suggests the folds may be due to muscular activity of urethra and oesophagus. Against this (Popoff) (29) is the fact that they are present in the tube prior to the development of muscular fibres.

Wichman (15) considers that the folds are due to epithelial activity rather in a centrifugal than centripetal direction, describing "insinkings" of the tubal epithelium. I have seen nothing in the way of epithelial activity, causing mesodermic compression, to support this view.

The Tubal Wall. The walls of the early Müllerian ducts consist of undifferentiated cellular mesoderm, but as early as the 38 mm stage a layer of these cells arranged concentrically, - the anlage the circular muscular layer - can be seen. Throughout development this remains the best marked layer.

With the development of the fimbriae, the submucous layer, at first poorly marked, becomes more defined, but it is not until 110-135mm stage that three distinct layers as well as the submucous, an internal circular, an intermediate longitudinal and an external, poorly developed, circular are present.

Wendeler considers that by the 25-30mm stage a differentiation can be made out between the anlagen of the tube and that part of the Müllerian duct which in conjunction with its fellow will be completely absorbed in the formation of the utero-vaginal cavity. There is general conformity of opinion that the site of junction of these two parts is marked by the attachment of the Round or Hunterian ligament, all that part of the Müllerian duct internal to this point forming eventually the utero-vaginal cavity (see later).

This author, i.e. Wendeler, also describes three layers in the tube wall, in embryos of the 50-60mm stage as follows:-

- i. Under the flat peritoneal cells, is a layer of loose circular fibres the cells of which have large nuclei, poorly developed and elongated bodies, with irregular fasciculated processes.
- ii. A thick layer with cells arranged on the whole longitudinally, some among them resembling young unstriated muscle.
- iii. The innermost layer composed of round, and short oval cells, somewhat irregularly formed and of different sizes. These cells are closely crowded together and possess dark cell nuclei, which differentiate them from their surroundings.

In my specimens the ultimate histological findings agree with this description, but differentiation is not present by so early a date.

Twists and Undulations of Tubes. These consist of:-

1. Bends and twists affecting portions of the tube and consisting of (i) angling with alterations in the direction of the tube (ii) true twists or spirals.
 2. Undulations etc. affecting the tube as a whole without influencing its direction of growth.
1. (i) The early angling of the tube, whereby it comes to possess an upper and lower vertical, and an intermediate horizontal portion, has already been discussed and its significance and results noted. (ii) Spiral twists in the tube, as a whole, have been described by Nagel, Wendeler and Freund.

Nagel (19) describes these to be unequal growth between the tube and its mesentery, while Freund (30) considers that during the "wandering" or sinking down of the tube from the false -- true pelvis, a complete spiral is formed. This he describes as being "unfolded" after the 32nd week. Freund states in support of this, that with the low power microscope he has seen spiral folds in the mucous membrane of the tube. Popoff who quotes Freund fails to make out the $6\frac{1}{2}$ - $7\frac{1}{2}$ twists described by this latter worker, and himself notices little in the way of spiral twists, although after the 8th month of foetal life, he observes that an irregular spiral arrangement in the tube can be made out.

2. The undulations of the tube are well marked in many of my earlier specimens and are, I think, due to unequal growth of the tube and its supporting mesentery, as well as to the increasing mobility gained by the lengthening

of this latter as before described.

Wendeler describes the development of "hands" in the broad ligament which prevents its increase in length pari passu with the contained tube, and cause foldings of this latter, but these I have not been able to make out.

The Utero-vaginal Canal.

Union between the two Müllerian ducts in the genital stalk takes place by the 30mm stage. This union, at first, is incomplete and even at the 48mm stage, evidences of the double character of the utero-vaginal canal, can be seen in its lowest $\frac{1}{3}$.

As stated previously, in our opinion, the utero-vaginal tube is responsible for the development of uterus, cervix, vagina and vaginal surface of hymen.

It is now my intention to summarise the steps by which these changes are brought about, and to compare my findings and their interpretation with those of other workers.

The Uterus, is formed from the upper hollow portion of the fused Müllerian ducts, that portion of the duct internal to the site of origin of the Round Ligament being destined to be included in the fundus uteri.

The development of the ligaments of the uterus while not actually within the scope of this work, is so closely bound up with the formation of the uterine wall, that a brief description of their origin and relations will not be out of place here.

The uterine ligaments are four in number, the utero-sacral, the broad, ovarian, and the round ligaments.

The first three are of no very great interest and can be briefly disposed of. The last, in relation to the development of the uterine musculature and fundus, closely concerns us here.

The Utero-sacral ligaments have little developmental interest, and are outside the scope of this work. They are, in reality, peritoneal folds, their contained muscular and fibrous constituents arising as a modification of the subperitoneal connective tissue.

The Broad Ligaments. These are formed by the junction of the mesonephric portions of the urogenital folds with their contents.

The tubar mesenteries, in correspondence with the short growth caudally of their contained Müllerian ducts, at first can be followed only a short distance from their origin in the posterior abdominal wall. The formation of the mesentery does not advance strictly *pari passu* with the extension caudally of the Müllerian duct, and, even in the 28mm and 30mm specimens, in which this duct has reached its fellow of the opposite side in the midline, the tubar mesenteries cannot be made out as distinct structures, further than the lateral pelvic wall. The duct here reaches its fellow of the opposite side, by travelling round beneath the peritoneum of the lateral wall and floor of the pelvic cavity.

In the 38mm specimen, however, the tubar mesenteries turn medially as peritoneal folds, with their contained ducts, and fuse in the midline to form a sagittal shelf, stretching across the pelvic cavity, and dividing it into a ventral or utero-vesical, and a dorsal or utero-sacral segment. This peritoneal shelf constitutes the Broad ligament. The loose mesoderm present between the layers of this fold is not at first differentiated from that surrounding the contained tubes and utero-vaginal canal, but by the 48mm stage a special condensation surrounding the tubes and utero-vaginal canal is present, the anlage of the tubal and uterine musculature. A specialised, lateral portion of the broad ligament at its attachment to the pelvic wall, is known as the infundibulo-pelvic ligament, and according to Felix (IE), arises in the following manner:-

The urogenital fold divides into a series of portions. There is first a division into mesonephric and genital folds, and the former is again subdivided into tubar, gland and mesenterial portions.

Taking the mesentery portion first, this has been termed the diaphragmatic ligament of the mesonephros, as for a short time during development it unites this latter to the diaphragm. During the development of the mesonephros, this ligament is continually degenerating and being formed anew, *pari passu* with the degeneration of the cranial end of this former structure. This process will be repeated from segment to segment until an

obstacle occurs to end it, and this obstacle is supplied in the ovarian artery, the ligament therefore persisting as the infundibulo-pelvic fold. The gland portion, speaking of the urogenital fold, atrophies greatly in the female, to be included in the mesovarium, while the tubar portion, as we have seen, unites with its fellow of the opposite side in the Broad Ligament.

Ovarian & Round Ligaments.

The genital fold may also be divided into three portions, that occupied by the reproductive gland and a free portion at either end, or as Felix terms them the "progonal, the gonol and epigonal portions."

When the reproductive gland or ovary reaches the pelvis, the caudal pole lies on the posterior aspect of the genital cord, and the epigonal portion of the genital fold consequently unites the caudal pole of the ovary with the genital cord. The condensation of the mesoderm in the broad ligament, to form the primordium of the uterine musculature, is taking place and extends just so far that the point of insertion of the epigonal portion comes to lie on the surface of the uterine wall. In its interior, the mesoderm is condensed to form a cord - the ovarian ligament.

The Round Ligament.

The round Ligament according to Felix (IE), is formed by the inguinal fold, the prominentia inguinalis of R. Meyer (31A) - joining the crista inguinalis or small pro-

jection from the posterior aspect of the anterior abdominal wall. In the interior of the crista, from earliest times, according to this author, there is a mesodermic condensation - chorda gubernaculi.

In my specimen, these two small projections, i.e. the inguinal fold and the crista, can be distinguished for the first time clearly in the 15mm specimen, the latter as a broad low projection from the posterior aspect of the anterior abdominal wall, opposite to which arises, from the lateral aspect of the genital fold, the small tongue-like projection of the inguinal fold, in the interior of which the mesoderm is somewhat condensed. Union between these two processes forms the basis of the Round Ligament. (See Fig. 93).

As far as I can understand, Felix describes the out-growth of the plica inguinal - opposite and towards the crista inguinalis - as bringing about a junction between these two, across the pelvic cavity. Against this view Meyer points out:-

- i. That the two prominences do not lie in all embryos opposite each other.
- ii. In embryos of this age i.e. during the time of early development of the Round Ligament, the inguinal region wanders from the dorso-lateral to the ventro-lateral side, and to explain Felix's hypothesis, the crista and prominentia would require to have some definite attraction for each other.

Of its mode of origin and growth, unanimity of opinion has not been reached, but the following views may be mentioned.

R. Meyer states that the Round Ligament (male = gubernaculum) is present in both sexes by the 13mm stage, as a spirally curved, fibrous mesenchymatous band, which passes from dorsally, a

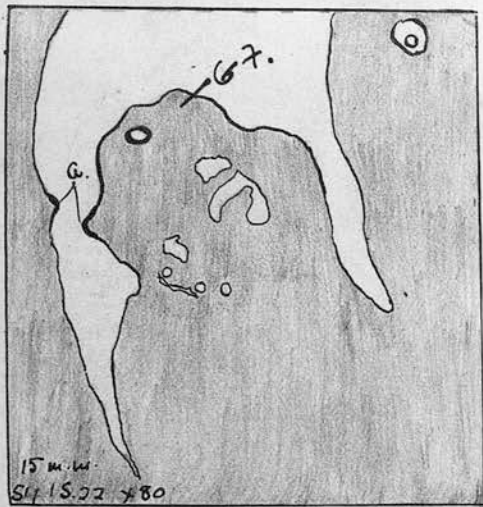


Fig. 93.

15 mm. embryo
x 80. to show
formation of
round ligament,
"a" = Crista &
plica inguinalis
G.F. = genital
fold.

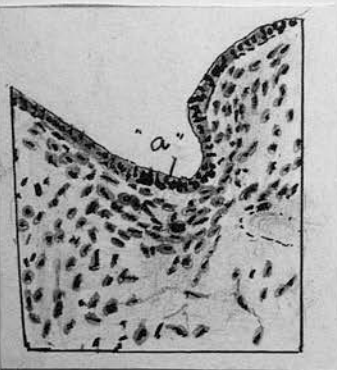
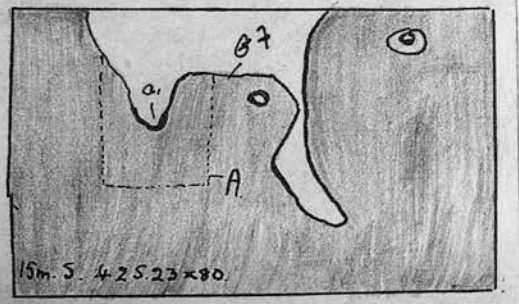
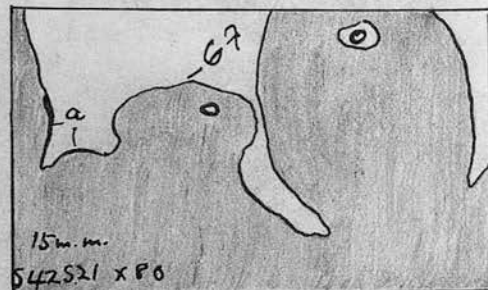


Fig. 94

15 mm. embryo
x 140. Area
A. from (Fig.
93 iii). en-
larged to show
condensa-
tion of
mesoderm
forming ba-
sis of round
ligament,
area "a".

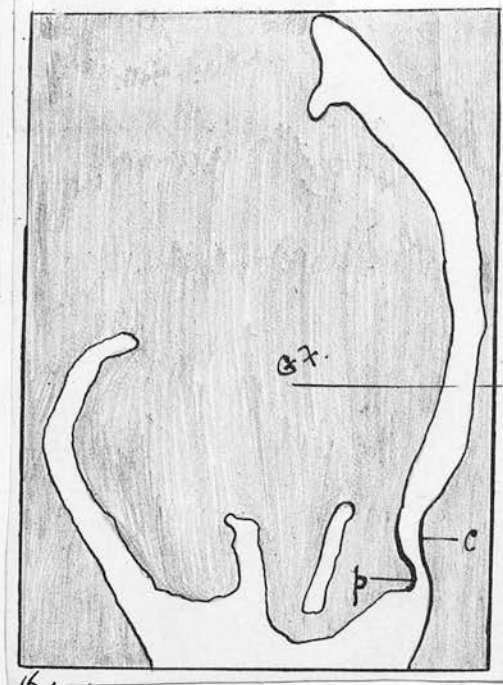


Fig. 95.

16 mm. embr
x 80. To sh
the crista i
guinalis "c"
and plica i
guinalis "p"
G.F. = geni-
tal fold.

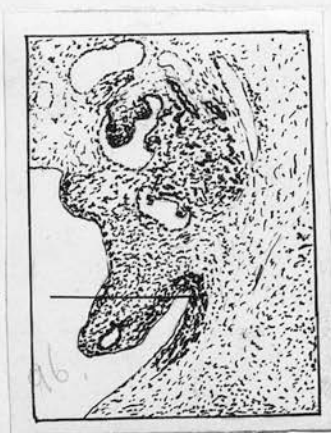
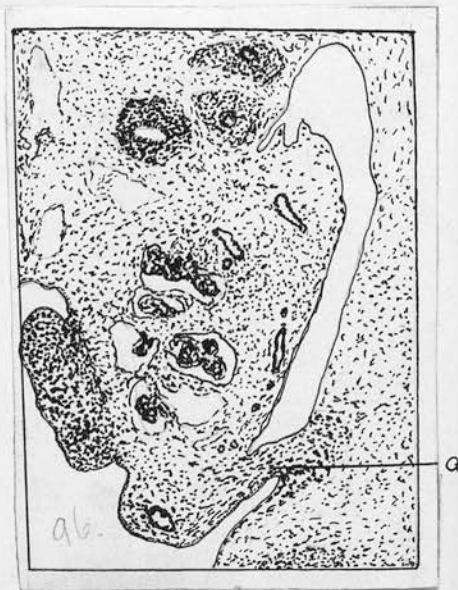


Fig. 96.

16 mm. embryo x 80. To show condensation in line of round ligament at "a".



small projection on the lateral border of the mesonephric fold, with its contained duct (prominentia inguinalis), to ventrally, a ledge which springs from the side wall of the peritoneal cavity near its posterior part (crista inguinalis). This worker describes how with the broadening of the abdomen in the region of the mesonephric folds, and its widening in the antero-posterior direction, the true pelvis remaining narrow, this spiral band is gradually opened out and the ventral point thus comes to lie near the region of the shelf which is at first far to one side; this comes towards the midline with the muscular development of the anterior belly wall.

Meyer emphasizes the fact that this "junction" does not arise anew but is rather a fibrous differentiation in the depths of the fold which originally existed between the side wall of the abdomen and the crista inguinalis.

Three parts of the ligament may thus be differentiated according to development.

- i. Promenentia inguinalis - Pars uterina
- ii. Portion lying in body wall, later included in broad ligament. - Pars lig. lata.
- iii. Pars inguinalis - inguinal part.

I certainly agree with Meyer that this junction, i.e. between the crista and prominentia inguinalis does not arise anew. In my specimen (see Fig. 94) at the time or shortly after the first appearance of these structures, a small band of cells can be seen uniting their parts via the lateral wall of the abdominal cavity.

Lubosch (32) states that he first saw the Round Ligament with certainty in a 20mm embryo as a Y shaped structure - the common ligament forming the base of the round ligament.

Kermauner (33) quotes Felix as describing the Round Ligament as an outgrowth from the Wolffian ridge = crista inguinalis, and Klaatsch (34) and Frankl (35) as a fold left after atrophy of the Wolffian Body. Against this latter theory Kermauner rightly puts the absolutely constant course of the ligament, and the facts that the lower pole

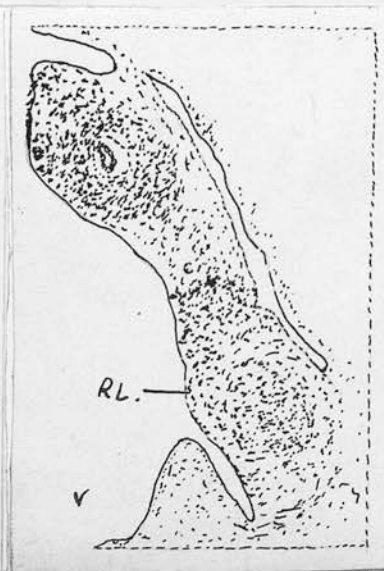
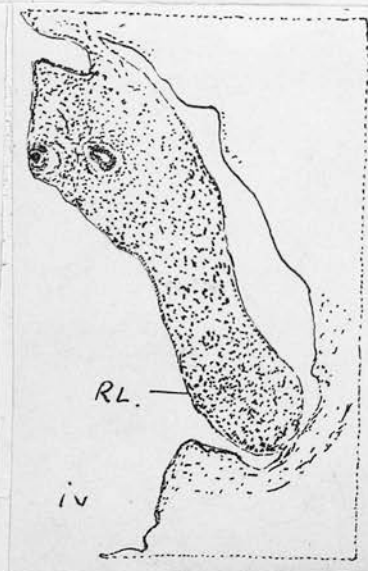
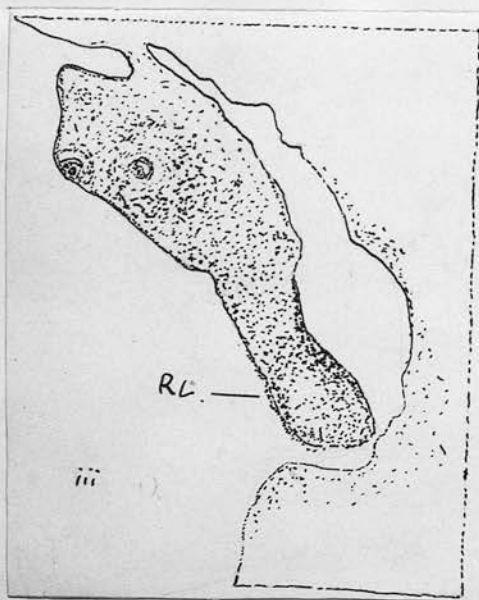
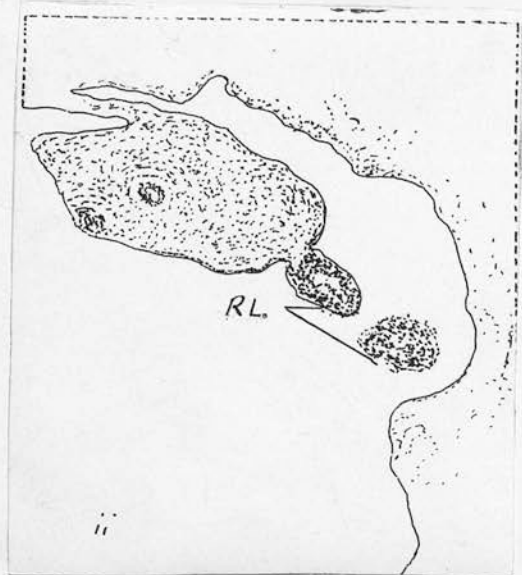
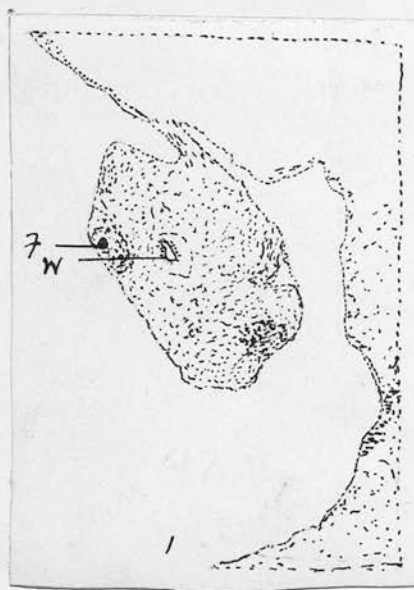


Fig. 97. 38 mm. embryo x 50. To show formation of round ligament (R.L.)
(F) = Fallopian tube (W) = Wolffian duct.

of the Wolffian Body only reaches the 2nd lumbar segment, and that it is unknown to find a peritoneal fold so rich in mesenchyme as this. Kermauner himself describes the Round Ligament as having its origin in the nephrogenetic fold (Gewebsstrang) and mentions that glomerular structures left behind developmentally may be the origin of adenomata of the round ligament.

In my own series of specimens the anlage of the Round Ligament is well marked by the 15-16mm stage in which slight low projections on the Wolffian or tubar mesentery and the lateral body wall, corresponding to Meyer's prominentia and crista inguinalis, are present (see Figs. 93 and 95). These two points are continuous round the postero -- lateral body wall, by a definite but not very marked band of cells (see figs. 94 and 96). As development proceeds with broadening of the body cavity and increase in depth in its antero-posterior diameter, these two points come to lie one before the other with a straightening out of the uniting band, corresponding with Klaatsch's view.

By the 38mm stage (see Fig. 97) the prominentia inguinalis lies directly ventral and continuous with the crista, the former is internal and shows an active core of growth, which is being surrounded by the growing musculature of the antero-lateral abdominal wall, with the formation of processus vaginalis.

While morphologically I think there is little doubt that the round and ovarian ligaments are continuous, this is in the female somewhat difficult to explain developmentally, and a careful examination of my specimens



Fig. 97A. 48 mm. embryo x 50. To show ovarian (OL) and round ligament (RL) (O) - ovary (F) = Fallopian tube.

has not revealed cells which can be traced through the broad ligament continuously from one structure to the other.

Klaatsch denies any genetic connection between the round and ovarian ligaments, but Wieger (36) considers that both bands are part of one structure and, in favour of this, describes muscular fibres passing from one to the other, and states that in congenital absence of the tube, which in my experience is extremely rare without the absence of the corresponding ovary, the round and ovarian ligaments form one continuous structure.

In spite of the various views as to the origin and mode of development, as I have said before, all workers are unanimous in considering that the cephalic site of attachment of the round ligament marks the junction of the tube proper and that portion of the Müllerian duct which ultimately joins its fellow, to form the utero-vaginal canal.

It is to be noted, however, that it is by spread of the condensation or specialisation of the mesoderm surrounding the utero-vaginal cavity outwards on the tube, that the inguinal fold, or round ligament derived from it, first comes into relation with the uterine wall. The ligament has nothing to do with the utero-vaginal canal.

Remembering this, Fig. 98 represents semi-schematically the resulting changes in the shape etc. of the uterine cavity from the earliest stages up to the 135mm embryo. It will be noticed that the cavity which was

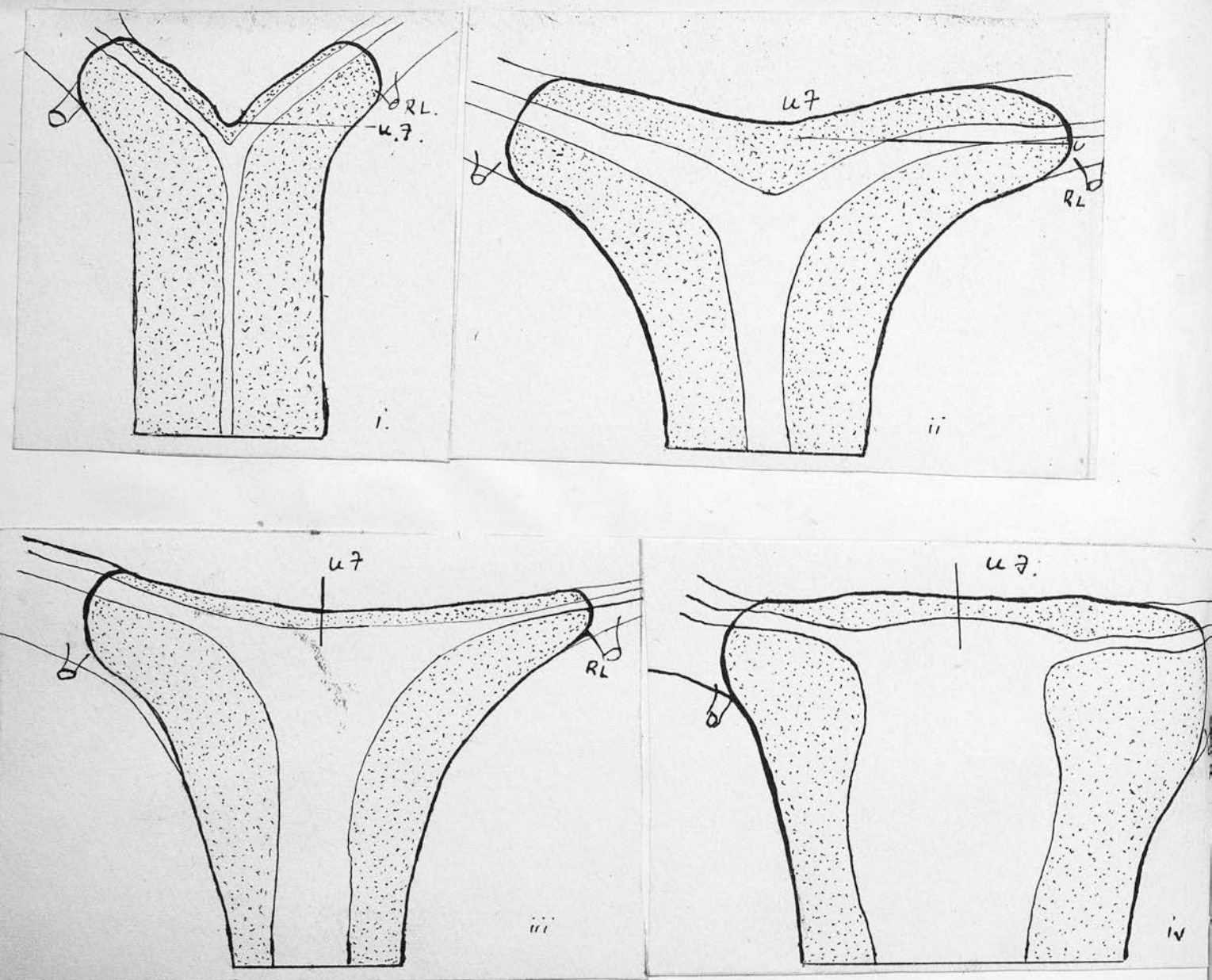


Fig. 98. Semidiagrammatic reconstruction to show formation and alteration in shape etc. of uterine fundus. (uf) RL = round ligament.
 (i) = 38 mm. emb., (ii) = 65 - 75 mm emb., (iii) = 110 mm. emb. (iv) = 135 mm. emb.

originally bicornuate assumes gradually the triangular shape present in the anatomically fully developed uterus, and this by absorption of the inner or uterine ends of the tubes into this latter cavity.

Coincident with this, and with the increasing development of the musculature of its walls, the uterine fundus, at first concave or V shaped in outline, becomes flattened and then slightly convex, this latter form, however, not being reached with any definition in foetal life.

The Uterine Musculature.

The muscle walls of the Müllerian tubes and uterus are derived from the mesodermic structures around them and are therefore continuous. This mesoderm surrounding the utero-vaginal canal is condensed to form the genital stalk, which in turn becomes differentiated to form the walls of the contained canal.

The cells forming the muscle wall of the uterus are not so clearly arranged into layers as those forming the tube walls but a well-defined basement membrane and submucous layer is present, and there is a layer of cells arranged circularly and continuous with the circular layer of the tube. The main thickness of the uterine wall, however, is made up of an irregularly arranged or retiform layer, the fibres of which show some tendency to be grouped round the blood vessels. These latter are, for the most part thin-walled, except where the large main uterine trunk ascends just external to the muscular wall to send branches into it.

Between the uterine(fundal) and cervical portion of the

uterine wall, little distinction can be made in my specimens in the structure of the musculature. This tends to be more irregularly arranged in the so-called cervical than fundal portion.

Clark (36A) working on the origin of uterine muscle in relation to blood vessels makes the following remarks:-

In the 3rd month of foetal life a few small spaces containing blood corpuscles are present in sections. In the mesometrium a few broader connective tissue strands and a large preponderance of delicate connective tissue are seen.

At 3½ months larger spaces with delicate fibrous lining are present, a few containing blood also fine arteries having the appearance of growing in from the broad ligament.

5th month. There are now endothelial lined spaces and small curling arterioles, with a muscular middle, and outer fibrous coat.

7th month. Venous spaces abound but arteries still mainly run in the parts of the uterine musculature near the broad ligament.

8th month. Arteries can be traced as far as the endometrium - have thick muscular walls and a more intricate outer fibrous coat.

By the completion of intra-uterine life, actual vascular ingrowth has proceeded as far as the endometrium, in the cells of which a few small arteries are seen.

From which Clark draws the following conclusions:-

1. During foetal life, the uterus has a trabecular arrangement and the arteries appear to grow into the trabeculae from the Broad Ligament. The venous spaces appear to arise in situ.
2. There is an extremely pronounced growth of the muscular tissue of the arteries in the uterus especially after the 5½ month.

Werth and Grusdew (37) have also done extensive and detailed work in the development of the uterine musculature.

These authors quote Sobotta (38) who states that there is phylogenetic agreement in the building of the uterine musculature from the circular layers of the tube which lies in close relation to the mucosa.

While I agree with this I differ from the statement which follows, namely, that in the 7th-8th foetal month, the uterine muscular wall is composed of circular fibres with absence of arrangement in layers, and that this is later converted into a network. In my specimens, while circular fibres in the uterine wall can always be detected, the trabecular or retiform layer always remains the major and more striking element.

Werth & Grusdew describe the development of the uterine musculature in the following stages:-

1. Premuscular period of wall of genital canal.

These authors quote Rösger (39) describing the presence of two layers:-

- a) An inner undifferentiated cell layer.
- b) Outer spindle cell layer.

In the youngest uterus in Werth & Grusdew's series, the uterine wall is composed of rounded cells extending practically to the cubical coelomic epithelium.

In the next stage, three clear layers can be distinguished in the uterine wall.

- a) Small peripheral connective layer
- b) Layer of small compact cylindrical cells
- Rösger's outer layer.
- c) Inner indifferent rounded cell layer.

By the 5th month the tube wall has definite muscular fibres arranged circularly. These pass over insensibly into the musculature of the corpus, the circular fibres of the two blending together at the uterine cornua and fundus.

As the result of investigation into the structure of the uterine muscular wall, Werth and Grusdew find this follows the same definite plan, from the earliest appearance of muscular fibres, and they are therefore of the opinion, in contra-distinction to Rösger, that the uterine musculature develops along certain constant pre-ordained lines. They also state that probably the course of the blood vessels has little influence in the direction of growth of the muscular fibres, which latter, the primordial uterine musculature, is a direct continuation of the circular tubal musculature and vice versa. With this last statement I am in agreement.

The mucosa of the utero-vaginal canal.

At the time of first formation of the utero-vaginal canal, i.e. about the 28-30mm stage, the lining of the tube is a simple low columnar or cubical epithelium, undifferentiated from that lining the early Müllerian ducts and similar throughout the utero-vaginal cavity. The cells filling up the distal solid portion of the canal are of a similar small rounded character.

By the 48mm stage, some differentiation has occurred, the cells lining the more distal part of the utero-vaginal tube just above its solid end (see reconstruction) (see Fig.37) tending to be of a definitely higher character, i.e. tall columnar, rather than low columnar or cubical. There is no sharp line of demarcation between these two types of epithelia in any of my specimens, one passing insensibly into the other.

Uterine and cervical glands. The epithelium lining the uterine part of the canal shows irregular undulations. These are present by the 79mm stage, and become rather more marked, but never, as far as my specimens extend, are these folds regular, nor is there any suggestion of uterine gland formation, however simple.

In the more distal cervical portion of the tube, matters are different. In the 110mm stage, well marked ridges and grooves in the formation of which the mesoderm takes part, are present.

By the 135mm stage these have become much more marked (see description and diagram of configuration of

interior of canal at this stage p. 56.). As was stated before, however, a wax cast reconstruction of the interior of the canal does not reveal any very regular folds suggestive of an "arbor vitae" formation.

In the 170mm specimen there are very definite epithelial depressions, which are branched and narrow mouthed - the rudiments of cervical glands.

In none of my specimens, however, have I been able to detect any regular epithelial groove or ridge formation as is present in the cervix of a child or young virgin, and for this reason, I think it probable that this is of late development if it occurs in foetal life.

Vaginal mucosa. As stated previously, the cells filling up the distal solid portion of the utero-vaginal canal are at first undifferentiated. With the commencing formation of the vaginal bulbs (i.e. by the 79mm stage), however, these cells have become large round and poorly staining, especially towards the centre of the "bulb". With the breaking down of these large cells, about the 135mm stage, to form a vaginal lumen, this is seen to be lined by squamous epithelial cells, which are sharply defined from the columnar epithelium of the cervix.

Nagel (19) describes the utero-vaginal canal as being lined by tall narrow cylindrical epithelium, while the lower solid portion is filled by large protoplasmic cells. It will be remembered that this author is of the opinion that the lower part of the utero-vaginal canal does not possess a preformed lumen, but is from the first a specialised portion of the fused Müllerian ducts, and that this solid portion is entirely responsible for the enormous solid epithelial growth at the distal part of the utero-vaginal tube.

Tourneux and Legay (21) are of the opinion that a preformed lumen probably existed, and that this was lost through approximation of the walls and possibly hypertrophy of the lining cells.

It has been pointed out that it is difficult to imagine the growth of the vagina with its enormous bulbs arising from the original very small, solid apex of the fused Müllerian ducts, and, from my own observation, I am inclined to think that the truth lies in a combination of Nagel's and Tourneux & Legay's views, viz: that from the first the distal part of the utero-vaginal canal is solid, possessing no pre-existing lumen, and that the solid area is increased in extent by hypertrophy of the cells lining the tube proximal to it. It must be understood, however, that in adopting this view, I am not including in the term "solid portion" the structures which I have described under the term vaginal bulb, and which I consider to be responsible for the lower $\frac{1}{3}$ only of the vagina. Moreover from my own specimens I cannot agree with Nagel that the cells of this portion are differentiated from the first. In my opinion the cells, both of the lumen-bearing, and solid portion, at first resemble the common Müllerian lining cells, and differentiation only occurs later.

Nagel's description of the simple "furrowing" of the epithelium in the upper or uterine part of the canal, with, by the 160-170mm stage, definite epithelial "in-sinkings", often branched in the more distal portion, agrees with my own. He places the appearance of the cervical glands considerably before that of the uterine, which, he states, may be present just before birth, or not until afterwards and which are probably variable in time of appearance.

Baumgartner, Nelson & Dock (40) examining a series of uteri from the 6-7th month -- 20th year, found uterine glands present as small simple rudiments by the 7th month, and state that they can be found at all stages after this. They describe the earliest glands as small irregular out-pouchings from a semilunar mucosal fold, present in the interior of the uterus at junction of corpus and cervix.

These later develop constricted necks and enlarged end-pieces, similar to the gland rudiments.

Nagel describes the glands of the cervix arising as solid epithelial processes in the second half of foetal life. Nagel 160mm, Tourneux & Legay 175mm.

Holzbach, quoted by Spuler (16) describes the fundal glands as arising from epithelial folds, with interruptions of these at intervals i.e. glands run for a time parallel to the surface of the mucosa. All authors are agreed in regard to the later and uncertain development of the uterine fundal glands.

With regard to the transition from the uterine to cervical epithelium, in my own specimens a gradual process, - Tourneux - Legay describe the uterine cylindrical epithelium, as diminishing in height from the 3rd - 8th foetal month, with a gradual transition to the cervical epithelium. Thereafter they state, the transition is sudden.

section being present.

On the other hand the transition from cervical to vaginal epithelium, i.e. from the columnar epithelium of the distal hollow portion (cervix) to the squamous epithelium of the succeeding portion of the utero-vaginal canal (vaginal) takes place slowly and gradually but irregularly, i.e. possibly at a higher level anteriorly than posteriorly, or with the presence of islands of squamous epithelium among the columnar epithelium, or vice versa. This definite epithelial change is certainly present by the 79cm stage, probably before this.

The structural formation of the cervix, however, is of a much more complicated nature and I think it will

Development of the Cervix.

I have purposely omitted a detailed description of the development of the cervix up to this point, to avoid confusion and because I have few specimens which are helpful in elucidating the processes concerned.

It has been indicated in the foregoing descriptions of specimens that histological differences in the lining membrane of the utero-vaginal canal exist as early as the 48mm stage. In the hollow proximal portion of this tube there is an upper or cephalic portion lined by rather lower columnar or cylindrical epithelium, which can be differentiated from the narrow more distal portion, lined by higher columnar epithelium. The transition from one type of epithelium here to the other, as has been remarked, takes place gradually, no hard and fast line of demarcation being present.

On the other hand the transition from cervical to vaginal epithelium, i.e. from the columnar epithelium of the distal hollow portion (cervix) to the squamous epithelium of the succeeding portion of the utero-vaginal canal (vagina) takes place clearly and suddenly but irregularly i.e. possibly at a higher level anteriorly than posteriorly, or with the presence of islands of squamous epithelium among the columnar epithelium, or vice versa. This definite epithelial change is certainly present by the 79mm stage, probably before this.

The structural formation of the cervix, however, is of a much more complicated nature and I think it will

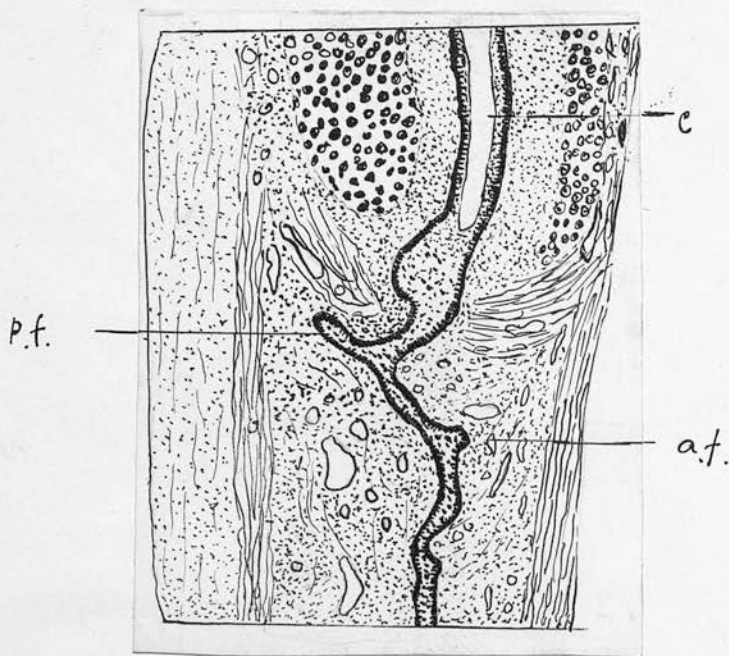


Fig. 99. From Werth & Grusdew's paper (37) p.412. 260 mm. (Crown Hee
embryo to show formation of portio vaginalis. (p.f.) = anlage
post. fornix, (a.f.) = anlage of ant. fornix (c) = cervical ca

be best to give a short description of the generally accepted view of development, and then compare this with my own rather scanty material and the views of other workers.

Quoting from Felix (1F) (Keibel & Mall), "In the 3rd - 6th foetal month the portio vaginalis is formed by the following processes:- first, the utero-vaginal canal thickens in all its dimensions, even in the third month, and second, the epithelium forms, at the junction between the cervix and vagina - but always in the vaginal territory, - a ventral and dorsal solid projection, which grows out into the mesenchyme in a shovel-shaped form. They are the solid anlagen of the fornix anterior and posterior vaginae, and therefore bound the anterior and posterior lips of the external os uteri (see Fig. 99).

The projection that represents the anterior fornix is always considerably lower than that representing the posterior fornix. With the anlage of the portio--vaginae or of the two fornices, the upper limits of the vagina become sharply determined. Only after the formation of the fornices does the vagina become hollow by the breaking down of the central cells, and the arrangement of the peripheral ones into a stratified cubical and later a stratified pavement epithelium. Starting in the distal portion, the breaking down of the central cells proceeds caudally. In this manner the vagina, together with the two fornices, becomes hollow and the protuberant portio-vaginalis is grooved out from its surroundings.

From the specimens at my disposal, I have not been able to fully convince myself of the exact mode and time of development of the cervix. These specimens include the pelvic organs of the following fetuses cut (A) transversely, and (B) Vertically. In the first column the measurements are given in Vertex Breech measurements while in the second corresponding Crown Heel measurements are shown.

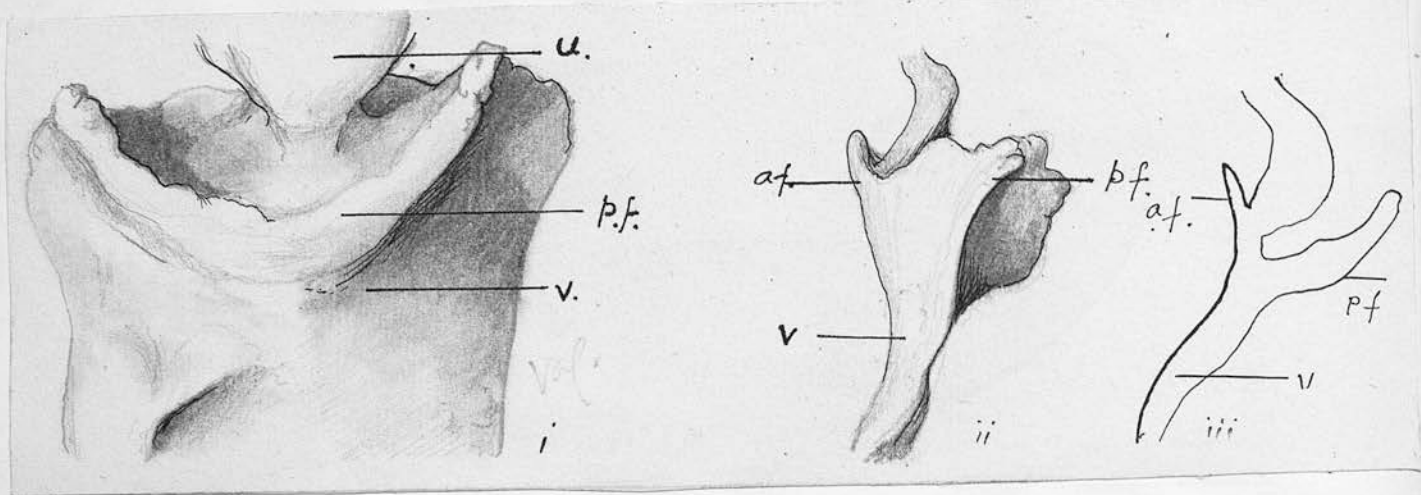


Fig. 100. (By courtesy of Professor Frazer) 170 mm embryo. Reconstruction formation of cervix. (i) from the back (ii) from the side. (iii) plan (u)=uterus (v) = vagina, (p.f.)=epithelial outgrowth to form post fornix, (a.f.) = epithelial outgrowth to form ant. fornix.

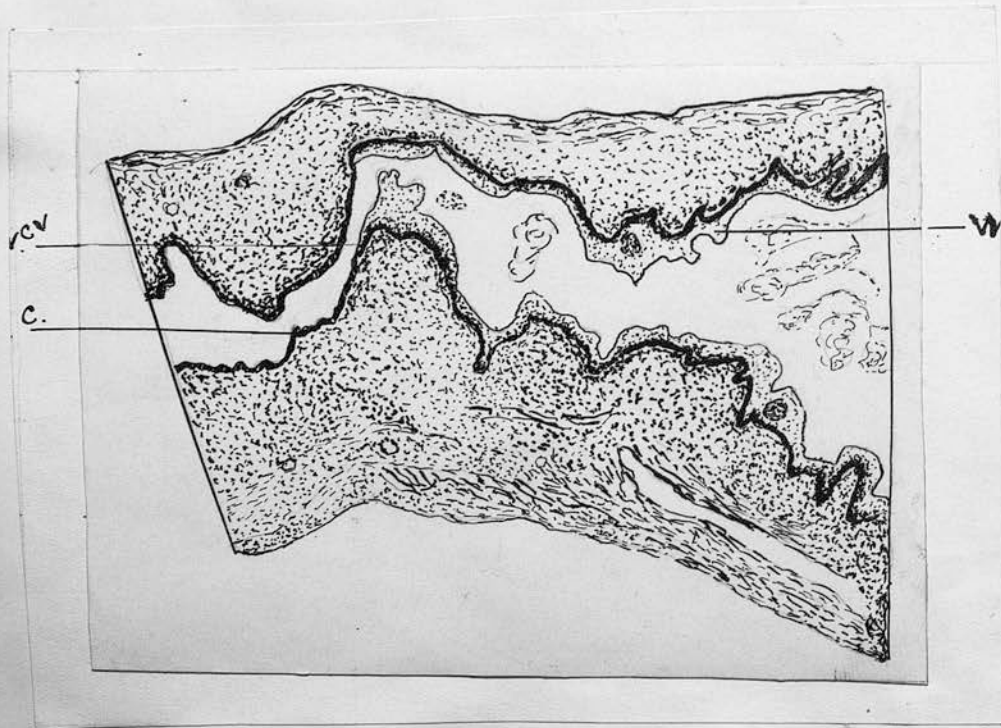


Fig. 101. 190 mm. embryo x 30 - Cervico - vaginal junction (c.v.), (c.) = cervical epithelium (v) = vaginal epithelium.

	<u>Vertex Breech</u>	<u>Crown Heel</u>
A	79 mm	115 mm
	110 mm	148 mm
	165 mm	200 mm
	170 mm	250 mm
B	105 mm	+ 140 mm
	110 mm	150 mm
	190 mm	290-300 mm.

In my 79, 110, 135 and 165 specimens, vertical reconstructions were made, but no evidences of vaginal fornices, in the form of anterior and posterior epithelial spurs growing out into the surrounding mesoderm, can be made out.

The appearances in the 170, (i.e. 260 Crown Heel) specimen are more suggestive, and diagrams and reconstructions are therefore shown here. From (See Fig. 100) it will be seen that a spur or shelf of epithelium is growing out from the solid vaginal portion of the utero-vaginal tube, to form the posterior fornix vaginae,

In the 190mm specimen (Crown Heel 290-300) the lumen is present in the vagina and the lining membrane of the cervix is sharply but irregularly defined from that of the former canal. The appearances here (see Fig. 101) agree with, and closely resemble those illustrated for a 315mm specimen, in Werth & Grusdew's paper.

An examination of the literature shows, in general, some conformity of opinion in the mode of development of the cervix, the description given by Felix being the most universally accepted.

The time of occurrence and exact method of origin of the various processes concerned, have, however, been very differently interpreted, see Spuler (16).

Kussmaul gives the time of origin of the cervix as the 3rd month, while Nagel (see later) mentions the 120mm - 140-150mm stage.

Tourneux & Legay give as the most usual period the 120mm - 150mm stage, but add, as do most authors, that the time of formation is variable, and may be at any time from the 4th - 6th month.

Bayer (42) gives the 160mm stage.

Werth & Grusdew have found the formation of the cervix occurring in a foetus of 230mm (Crown Heel) towards the end of the 5th month while Geigel (43) mentions the 6th month.

Re the Mode of formation, this has been variably described as (i) A widening of the cranial end of the vagina, *pari passu* with the development of the boundaries of the cervix, or (ii) there is found in the yet small solid portion of the utero-vaginal canal, ("conus vaginalis" of Spuler)(a) a forward epithelial outgrowth or possibly a similar posterior outgrowth, according to others, or (b) a ring-like fold of epithelium. Tourneux & Legay, Nagel & Bayer are supporters of view (a) which my own observations agree with, V. Koelliker (44) and Van Ackern (45) agreeing with view (b).

Nagel describes, at the junction of the cervical and vaginal epithelium - see former description of epithelia lining this part of utero-vaginal canal - or just distal to it, a sickle-shaped ingrowth of epithelium into the back wall of the genital cord. He states that the exact stage in time for this appearance is difficult to define, but that he has seen it at the earliest at the 120mm stage, but occasionally it is not present by the 140-150mm stage.

Once laid down, the sickle-shaped epithelial ingrowth grows rapidly and reveals the form of the posterior cervical lip. A similar epithelial ingrowth takes place into the anterior wall of the genital cord. These epithelial ingrowths take place at the site of the angle of the original bend of the utero-vaginal canal. Nagel states that the posterior lip is usually formed before the anterior, but occasionally vice versa or at the same time.

Occasionally there is a slight projection inwards at the site of the future of the anterior cervical lip, suggesting that possibly the anlage of the anterior lip is of earlier occurrence, but that full development of the posterior cervical lip is reached first.

Nagel describes "insinkings" similar to those which I have described, into the epithelium of the cervical canal. These he has followed in all stages from simple furrows to more complicated branching depressions, and he is of the opinion that they are the anlagen of the cer-

vical glands. Tourneux & Legay, however, consider they lead to the formation of the "Arbor Vitae".

These latter authors consider that the columns of the "arbor vitae" are present by the 75-105 mm. stage in the formation of the utero-vaginal canal.

S.E. Wichman's (15) description of the development of the cervix coincides fairly fully with the above. He states that differences in the cervical and vaginal epithelium can be recognised by the 3rd - 4th month, and that the border between the two lies within the cervical canal. The vaginal epithelium is developed, however, before the cervical mucous membrane is fully differentiated. By the 6th month the cervical epithelium develops and pushes the flat vaginal epithelium out of the cervical canal. Rests of vaginal epithelium, he states, may remain in the deep parts of the cervical epithelium and at birth, in about 50% of cases squamous epithelium reaches up into the cervical canal.

Robert Meyer's (31B) findings relative to the area of contact between the cervical and vaginal epithelia are interesting in this connection. He states briefly :-

- 1) Epithelium of vagina and cervix can be very early distinguished by the cell formation, i.e. 3rd - 4th month. The line of epithelial differentiation lies within the cervical canal.
- 2) The epithelium of the vagina develops into a multi-layered, flat, epithelium reaching the cervical canal. This epithelium is usually fully differentiated before the cervical epithelium commences to form a mucous membrane.
- 3) Cervical epithelium develops fully from the 6th month, and pushes the squamous epithelium out of the cervical canal. In some cases the exclusion of squamous epithelium out of the cervical canal takes place on to the external aspect of the cervix - forming the congenital pseudo-erosion.
- 4) Remains of squamous epithelial cells underlying the cervical mucous membrane multiply and cause breaking down of the epithelium of the portio. Sometimes even at birth, the site of differentiation between the two epithelia is not sharply cut, but still irregular.

In general, the earlier the differentiation of the cervical mucous membrane, the wider the area, and the greater the likelihood of pseudo-erosion and vice versa. Regeneration of the squamous epithelium of the portio, takes place through the basally remaining cells.

The Development of the Vagina.

The developing vagina has already received considerable incidental notice and partial description in the course of the account of specimens given in previous sections.

(A) So far as the upper and major part of the tube is concerned it is not necessary to add descriptive detail, but, for the purposes of continuity, a brief recapitulation of the formation of this part is desirable.

As mentioned in the 48mm stage, the lower part of the utero-vaginal tube forms a solid mass, but above this, the tube contains a lumen lined by columnar cells, which become more cubical in the higher parts. This single-layered lining appears to be the earliest character of the upper part of the future vagina and utero-cervical canal, but it is impossible at this stage to draw a line of demarcation.

As development proceeds, the changes incident in the lower part of the tube appear to extend upwards, and little points of proliferation are seen here and there, in the single layered lining. These gradually enlarge, and at the same time, the structure widens from side to side, in conformity with the general growth of the pelvis. In this way, the upper part of the vagina becomes flattened from before backward, and widened from side to side, its lumen being completely lost by approximately the 110mm stage. This solid epithelial vagina presents many points of "cell-nests" throughout it, from which - as centres - the squamous change in the lining appears to take origin.

Thus then, when a lumen is beginning to appear in the

vagina (about the 135 mm stage) by vacuolation of the central cells, the tube so formed has a squamous epithelial lining. Possibly from the disintegration of the cells of the epithelial nests just mentioned, grooves are formed which later lie between the folds of the columnae rugarum.

(B) The lower part of the vagina requires more detailed description. Our views on the development of this structure have been expressed in our paper (see The Development of the Lower End of the vagina & Hymen, J. Ernest Frazer and Alice Bloomfield, p.23 et seq.) which I now quote.

The views which we hold, as the result of our observations on the material, may now be briefly summed up. They are as follows.

1. The lower end of the vagina, like the rest of that structure, is purely a Müllerian derivative.
2. It establishes contact with the urogenital sinus at an early stage, at the apex of the "Müllerian tubercle". This site is that of the upper part of the future hymen.
3. Its lumen is for a time filled up by a plug of epithelial cells, derived from the lining cells of the canal. Later, by their active growth, these cells lead to the formation of the so-called vaginal bulbs. These bulbs increase the area of vaginal contact with the sinus (and become the hymeneal area) by their extension in a downward direction along its posterior wall. At the same time they invaginate this wall from behind, so that the sinus undergoes a relative diminution in length and a

change in direction of its long axis, a corresponding increase occurring in its opposite diameter. The hymeneal site is thus made to approach nearer the surface.

4. The hymen is formed passively by the invagination of the posterior wall of the sinus, as just described. Thus it consists of three layers - a layer of vaginal cells from the invaginating "bulbs", a covering layer of epithelium from the sinus, and an intervening stratum of vascular mesoderm which appears to be derived from the vascular condensations surrounding the walls of both these cavities.

5. The Wolffian ducts take no part in the formation of any portion of the vagina and hymen. They disappear in their lower parts (as a rule) at a fairly early stage, and when persistent, can be followed as small patent tubes which open near the free border of the hymen. This position on the hymen is due to their terminal openings being invaginated with that part of the sinus wall in which they are situated, and any secondary change leading to an opening beside the hymen would evidently be due to disappearance of the thin covering of sinus cells which lies over their invaginated ends.

In comparing these results with those of other observers we are faced with the difficulty of classifying the diverse opinions for purposes of review. It is only possible to do this in a very general way, owing to the overlap in many details, and perhaps the large division into three main classes, which we mentioned earlier in

this paper, affords as good a basis as any, on which we can make the comparison. These three headings were:

- (a) Descriptions which give the derivation of vagina and hymen as purely Müllerian.
- (b) Those which make it mainly Müllerian, but bring in an additional element in the development of its lower part. This new factor may be derived from the Wolffian ducts or from the urogenital sinus, entailing an associated origin for the hymen.
- (c) Those which derive the vagina mainly or altogether from the urogenital sinus, with similar hymeneal origin.

The difficulty of placing any individual opinion in its proper class can be exemplified in the present case; the views we advocate would certainly seem to belong to class (a) in the list just given, but, strictly speaking, the sinus-element in the hymen would give some reason for placing them also in (b).

- (a) R. Nagel (19) is one of the main supporters of the entirely Müllerian origin of the vagina. He described it as arising wholly from the united Müllerian ducts, the lower ends of which, becoming solid, grow rapidly in length through hypertrophy and multiplication of their lining cells, and come to invaginate the posterior wall of the urogenital sinus. The apex of the projection so formed breaks down to allow communication between vagina and sinus, this marking the site of the future hymeneal orifice - in the position of the Müllerian tubercle of earlier specimens. In this way the lower solid portions of the Müllerian ducts form the vagina, a lumen being absent throughout. This view, it is evident, is, in essentials, the same as that which we put forward, as is also his description of the formation of the hymen, which he considers to arise passively by the bulging of the Müllerian vagina into the sinus, invaginating it. He considers that active growth of the hymen may take place later, as shown by the fact that the hymeneal orifice may be relatively smaller in the new born child, than at any period in foetal life. This is, however, difficult of proof, and does not affect the main issue as to the mode of development of the hymen. While Nagel describes a bulging of the lower end of the vagina, the vaginal bulb-formation, which is so striking in our specimens, is not mentioned, nor the process of spread of the vaginal area of contact with the sinus, brought about

by this means.

Wood Jones (46) describes this Müllerian downgrowth as double, and in the form of bulbs. According to him, the fused Müllerian ducts reach and open into the upper end of the sinus at a comparatively early stage. Later this opening is lost, to be regained at an advanced stage of foetal life, this second opening being brought about by a paired bulbar downgrowth from the fused Müllerian ducts. These bulbs tunnel their way along the mesoderm behind the posterior sinus wall, to open at a much lower level than the primary opening, the hymen being that part of the mesoderm lying between this paired bulbar downgrowth and the surface, and at first unaffected by it.

While this view is distinctly comparable with ours as here expressed, we should like to say that we have never in any of our specimens seen any trace of a paired downgrowth in the mesoderm posterior to the sinus and not in contact with its wall. Wood Jones does not make it clear, when he states that the primary opening between vagina and sinus is lost, whether an epithelial contact is maintained, but we take his meaning to be that all communication between the two channels and their epithelia is lost, and opinion which we have found by our specimens to be erroneous. Contact having once been established between the vagina and sinus, at the 30-38mm. stage, is never again lost, but continues to increase in area by the formation of the vaginal bulbs and their downgrowth along, and in contact with, the posterior sinus wall.

According to other authors (with whom we do not disagree) the original utero-vaginal canal takes a much

larger share in the formation of the vagina, which possesses at first a lumen, lost through transition of the simple lining epithelium, into a multilayered squamous epithelium, the lumen of the canal being lost through growth of its anterior and posterior walls.

Felix (1F) describes this epithelial transition also, mentioning the appearance here of large rounded cells, which fill up the utero-vaginal canal and render it solid. The origin of these cells has caused much speculation, Felix considering that they arise from the cells lining the Müllerian ducts, while Berry Hart (47) derives them from the so-called Wolffian Bulbs, and Van du Hoeven, as quoted by Mijsberg (27) derives them from the lining membrane of the urogenital sinus. This places the views of these last two observers in our next group (b)

Before passing on to consider this group in detail, a few further remarks must be made on the "vaginal" view of the origin of the hymen.

Taussig (48A) in his original paper bases his views on five embryos examined by serial section, and considers the hymen has a vaginal origin independent of the place at which the vagina breaks into the urogenital sinus. Within this latter site arises a fold of vaginal tissue, the hymen. At the point where the vaginal bulbs break through, i.e. at the Müllerian tubercle, another more or less well-marked fold of tissue is left, which becomes obliterated as development proceeds. Taussig thinks that the bi-lamellate utero-vaginal hymen, which Schaeffer (49) describes as being found in so large a proportion of his specimens, is due either to an abnormal persistence of these two folds, or to the fact that many of the specimens were examined at a stage when both folds would be normally present.

Taussig in a later paper (48B) states that the hymen is not a passively formed structure, but that it is an actively proliferating outgrowth, and considers that such variations in the normal hymen, such as hymen cribriformis, can only be explained on such an hypothesis. We consider that such a variation as a cribriform hymen, could very readily arise by a process of passive bulging of the posterior sinus wall by the actively bulging vaginal bulbs, rupture and communication of the two contiguous lumina taking place not at one point but

at several, on the apex of the epithelial covered promontory so formed.

Taussig's second paper is largely based on vaginal and hymeneal abnormalities and, as these will be discussed later, nothing further need be said now about them.

Blair Bell, when asked to discuss Taussig's view, stated that he considered the hymen to be the remains of the urogenital plate, or anterior portion of the original cloacal membrane, but considered the question not proven as to whether it were a new formation or a disappearing membrane.

Gellhorn (50) is in agreement with our view and with that of Nagel, that the development of the hymen is inseparable from that of the vagina, and is formed by a bulging of the vaginal bulbs into the sinus. He, however, derives practically the whole hymen, with the exception of a thin epithelial covering from the sinus lining, from the vagina, considering that mesoderm from the vagina only grows into this. We are of the opinion that a true ad hoc invagination of the posterior sinus wall occurs, and that the mesoderm of the hymen is derived both from that of the vagina and of the urogenital sinus.

We have never seen any evidence of a vaginal hymen arising as an active fold of mucous membrane, and consider that the microscopical appearances are quite against such a view. The lumen of the lower end of the vagina (i.e. in the region of the vaginal bulbs) is filled with vacuolated desquamating epithelium, all activity of growth taking place at the outer limit of the epithelial mass, towards the surrounding mesoderm, and the urogenital sinus.

Among the more recent observers whose views must be placed in this class are Küstner (51) and Lubosch (32B). The former considers that the hymen arises at the site of the early Müllerian tubercle, taking as proof of this the fact that where the Wolffian duct is persistent, it opens on the hymen, i.e. its original site in embryonic life. His paper is largely based on a study of abnormalities, and he considers that such an error of development as the presence of the hymen in the absence of vagina is rather against his views expressed above. He states, however, in this con-

nection, that the hymeneal relations vary with the degree of development of the Müllerian ducts.

Lubosch describes the formation of a bulging lower end of the vagina, which invaginates the posterior wall of the urogenital sinus, the hymen thus coming to be formed passively, as we have described in our paper. He describes, however, the limiting of the spread of the bulging epithelial vagina, by a ring-like narrowing, which is continuous with the columnae rugarum and which he calls the "plica retrohymenalis." We have remarked no such specialised structure in our specimens.

We now come to the second class (b) of hypotheses about the development of vagina and hymen, namely that the former is mainly a Müllerian structure, but an additional factor is present in its formation and in that of the hymen.

(b) Berry Hart (47) is one of the best-known exponents of this view. He considers that the upper two-thirds of the vagina arises wholly from the fused Müllerian ducts, while he ascribes to the "Wolffian bulbs" - i.e. the lower ends of the Wolffian ducts, which he describes as becoming solid and developing bulbar enlargements on their extremities - the formation of the lower third of the vagina, the lining membrane of the entire vagina and the hymen, which therefore, in his opinion, forms below the site of the former Müllerian tubercle, i.e. at the original site of entry of the Wolffian ducts into the urogenital sinus.

Before proceeding to show how entirely we disagree with this view, those of some other observers, holding somewhat similar opinions, must be examined.

Tourneux and Legay (21) also mention the presence of "Wolffian bulbs" and consider they form the lower third of the vagina.

Mijsberg (27) whose recent and most interesting paper was published while this research was in progress, is of the opinion that the upper two-thirds of the vagina is Müllerian while the lower third is formed by the fusion of the Wolffian bulbs with each other, with the Müllerian vagina above, and the sinus below, while the hymen forms as the result of the reaction of the sinus to the growth in length of the vagina - here, in a limited

sense, in agreement with our view - and is therefore in actual structure, according to Mijsberg, partly of Wolffian and partly of sinus origin.

Against these views the very definite evidence of our specimen and reconstructions must be placed. At no stage and in none of our specimens have we seen any evidence whatever of Wolffian bulb-formation. In many of our specimens it was possible to trace the Wolffian duct to a lesser or greater extent. In the former case, with one exception, the Wolffian duct was always lost sight of as a patent duct, possessing a lumen, lined by a single layer of cubical epithelium, and without any evidence of proliferation of these lining cells or of bulb-formation. In the exceptional case, the Wolffian duct was seen on one side to join, or rather come into contact with, the outer side of the Müllerian bulb-formation. No cells, however, were given from the Wolffian duct, to this bulb-formation, which had already reached a developed state above the level of contact, and the duct was completely lost sight of in the next - serial - section. In cases where the duct could be followed to the sinus its lumen was maintained throughout, and it opened into the urogenital sinus below the opening of the fused Müllerian ducts. This is particularly well seen in one - 170mm. - specimen, where a patent Wolffian duct on either side is seen to open into the sinus on the surface of the hymen. R. Meyer (31B) has also traced the duct opening in this position.

In addition, against the view put forward by Berry Hart - that the hymen forms below the site of the original Müllerian tubercle - we consider that we have conclusive evidence in our specimens and the reconstructions made therefrom, that the fused Müllerian ducts, having once established contact with the sinus epithelium at the apex of the Müllerian duct, never again lose that contact (and at this site the hymen is formed) but continue to increase it, and the area of the hymen, by the formation of the Müllerian or vaginal bulbs.

Other workers who in addition to R. Nagel, already quoted, agree with us in attributing a "unilamellate" vulvo-vaginal origin for the hymen, are Budin (52) and Webster (53). Budin, basing his work on dissections of adult specimens, considers that the hymen does not exist as an independent structure, but that it is merely the projecting lower and anterior end of the vagina, while Webster describes the hymen as the septum which is left between the urogenital sinus and the lower part of the vagina, as the latter becomes channelled, the opening of the hymen being formed by the involution of the epithelium on the urogenital surface of the hymen.

Spuler (16) considers the vagina mainly Müllerian, but thinks that the lower fused ends of the Müllerian ducts, here called the "Conus Vaginalis," derive cells from the urogenital sinus, and that the lower third of the vagina arises by a frontal division of the urogenital sinus, which brings this worker into line with the next group, (c) in which the sinus is held to play a large and important part in the development of the vagina.

(c) Retterer (54) describes lateral folds arising in the sinus wall, about the fourth month of foetal life. By union of these folds from above downwards, the lower portion of the vagina is formed, the upper part i.e. that in relation to the base of the bladder, being formed from the Müllerian ducts.

Pozzi (55) also agrees that the lower third of the vagina is derived from the urogenital sinus.

The latter bases his belief largely on a study of vaginal and vulvar abnormalities, especially on a case in which a hymen was present but no vagina. The vagina was represented by a small pocket only,

which he considers to be the lower part of the vagina, derived from the urogenital sinus, which also gives rise to the hymen. Other abnormalities of development put forward to support this view are :-

- (1) The presence of a single hymen with a double vagina.
- (2) The presence of a hymen or fold which surrounds urethral as well as vaginal orifice.

On the general question we would like to point out that theories of development based on mal-developments are only satisfactory when the assumptions are borne out by normal embryological investigation. At least, they should not be in opposition to what is observed in normal development. It is not usual to find the hymen in the absence of the vagina, but there is nothing in its presence under these conditions to invalidate or disprove in any way the facts observed in the study of a normal sinus. The urogenital sinus has many folds, and these can be followed from their inception to what is practically the attainment of the definitive condition, but we have certainly not seen any stage, nor have we been able to come across any description, in which one or more of these folds is clearly shown to form a hymen. On the other hand, the hymen can be seen to be formed at the contact-region of vagina and sinus. It would seem much more likely that, in these cases, the lower end of the vagina and hymen were made in the way indicated above and that subsequently and for some reason in any case unknown, vaginal atrophy occurred. So far as we know, no dissection has been undertaken on such an abnormality to determine the presence or absence of remnants

of a vagina

With regard to the second abnormality, double vagina and single hymen, this would seem to admit of a very simple explanation. The double character belongs to the vagina, and, as has been shown, is still evident to some degree at the lower end, even when this is growing. Nevertheless, the growth, as a whole, invaginates the wall of the sinus and produces the hymen, and it does not require much imagination to see that it is quite possible for the double character of the vagina to be much more marked and persistent, while the effect of the growth of the structure, as a whole, is exercised in the production of a practically unpaired projection into the sinus. Still more marked division, or want of fusion, of the vagina, and distinction of its bulbs, would lead to a definitely double invagination, from which would be derived the commoner variety of double hymen with double vagina.

The presence of a hymen surrounding the urethral orifice as well as that of the vagina does not appear to invalidate in any way the account given of the formation of the parts. In fact, during the course of this investigation, we have noted with interest the presence of a definite invagination of the posterior and upper part of the sinus wall implicating the urethra as well as the vagina. In this way a common hymen might be formed, although, as a rule, the structure ultimately becomes

vaginal. We have made some observations on this matter, but have not paid particular attention to the details, as they seemed to be rather outside the more fundamental scope of the questions we were trying to solve. An investigation of the whole development of the female urethra, particularly of its lower part, is needed; we did not go into the question, but what we observed has satisfied us that the presence of a hymen which includes the urethra may be an indication of an inhibition, but at any rate does not clash with the vaginal productional value of the ordinary hymen.

With regard to Retterer's view, we know that septum formation and division of the sinus are said to occur in certain animals (Mijsberg). We have not studied these, and are of course in agreement with most other observers, that such a method of development never takes place in the human embryo. The site of the opening of the Wolffian ducts into the sinus below the Mullerian vaginal orifice, disproves this theory. If the lower third of the vagina arose from the sinus, the Wolffian ducts should open into the vagina - unless indeed, as suggested by one author, they deviate from their close relation to the vagina at this point, extend down in the mesoderm external to the sinus, and come to open below the vaginal orifice formed as above. It seems hardly necessary to say that this effort of the imagination lacks any support whatever from developmental observation.

Before bringing this account to an end, we would like to call attention once more to the Wolffian ducts. On general principles one would expect to find the female tract associated with the Müllerian ducts, but, on some views as to their possible evolution, it does not seem justifiable to deny theoretically the possibility of some Wolffian intervention at the lower end. With such outlook we naturally paid particular attention to the nature and condition of any remnants of the Wolffian ducts with which we came in contact. In this matter we were struck by one common character possessed by all these remains; there was never any sign whatever, in any place, of any activity of the lining cells of the ducts. Their lining was formed by a single layer of cubical cells, surrounding a small lumen, except in those sections where the lumen was disappearing, the cells here coming into contact and getting smaller, and the whole structure plainly on the point of vanishing. In fact the only signs of activity seen were retrograde and directed towards atrophy and disappearance. At no time could we see the faintest sign that either duct might be about to form a bulb, was forming it at the time, or had formed it, and, whenever that duct could be traced to the sinus, it ran to its original site without any enlargement, and unconnected with the vaginal structures. We have spoken of the one case (Fig. 59) which seems an exception to this last statement, but the fact that it was the only case, and the appearance presented by the rem-

nant on examination, make it in our opinion clearly a case of accidental contiguity. Here and there, along the sides of the vaginal bulbs, are processes directed outwards and backwards, which owe their direction doubtless to the fixation of their ends in the surrounding condensation while their bases are carried forward by the growth of the bulbs. Such processes, when cut longitudinally, may be taken in our opinion - for Wolffian remnants, and we cannot help thinking that some such mistaken reading of a section may account for some of the description of "Wolffian bulbs". The fact that they may be fairly numerous, and that they may co-exist with the real duct, disposes of them at once. The successive stages that we have examined have given us pictures in which the outstanding impressions we have gained have been those of great activity in the Müllerian structures, and complete absence of activity of any sort, except atrophy, in the Wolffian ducts.

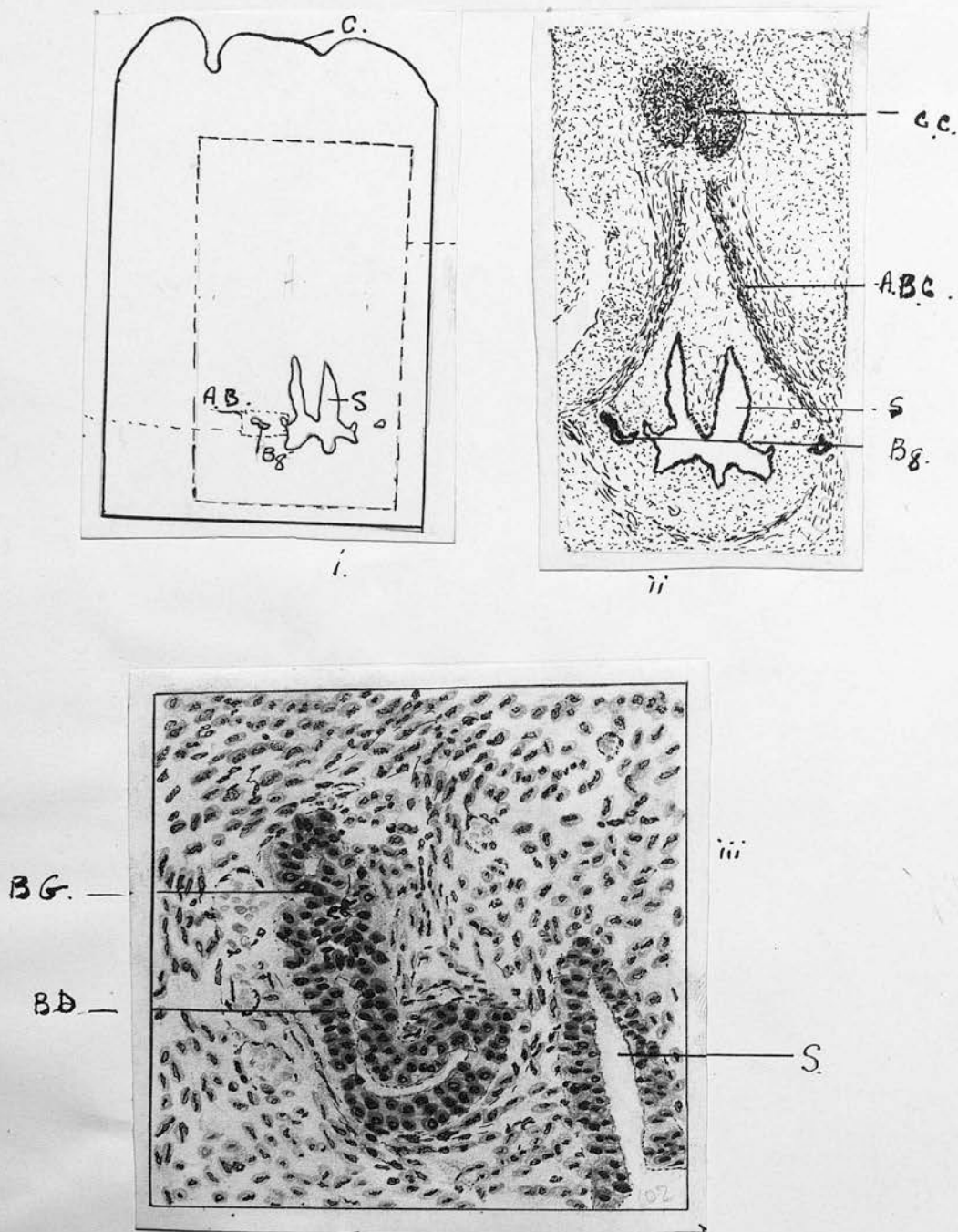


Fig. 102. 48 mm. embryo (i) x 30. To show relations of Sinus, Bartholin's gland = (B.g.), and clitoris = (c), (ii) x 50 to show area (A.B. enlarged, (cc) = corpus clitoridis, (ABC) = Anlage of Bulbo-cavernosus muscle, (iii) x 320 = area (AB) further enlarged to histology of Bartholin's gland = (BG), Bartholin's duct = (B.D. and Sinus = S.

BARTHOLIN'S GLAND

While the development of Bartholin's gland does not strictly come within the scope of this paper - its function is so closely bound up with Bartholin's groove and the latter's very important relations to the changing configuration of the sinus wall - that a short description will not be out of place here.

In the description of early specimens - we noted that the first rudiment of Bartholin's gland was present by the 28mm stage, as an epithelial thickening in the base of the then longitudinal groove B, henceforth known as Bartholin's groove (see Fig.19).

By the 38mm stage a definite glandular acinus or epithelial bud has developed. (See Fig. 31).

48 mm. Embryo.

Bartholin's Gland. In this specimen, both a lumen-bearing duct and gland acini are present arising from the anterior division of the bifid extremity of the groove "B". Bartholin's gland consists here of 2-3 gland acini, either solid or possibly possessing very small lumina, lined by high columnar epithelium. These join together to open into a duct, possessing a well-marked lumen lined by lower cubical epithelium. There is no definite mesodermic capsule, but the gland and its duct are surrounded by a layer of longitudinally placed cells apparently derived from a curious and well-marked longitudinal band of cells, which passes from the region

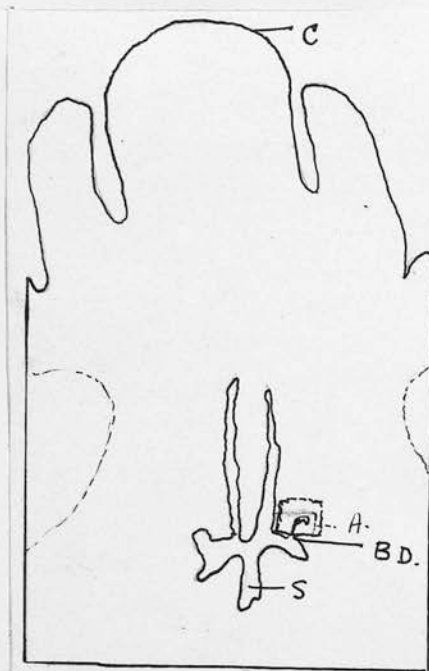


Fig. 104A.

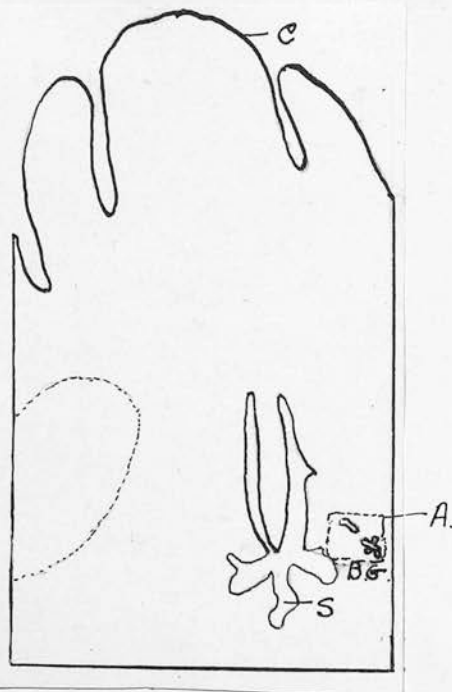


Fig. 103A.

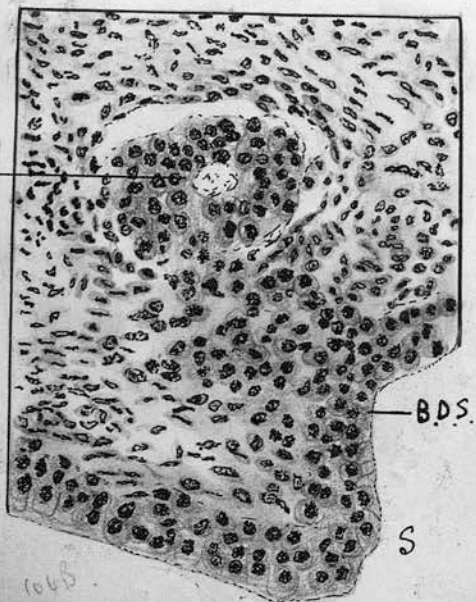


Fig. 104B.

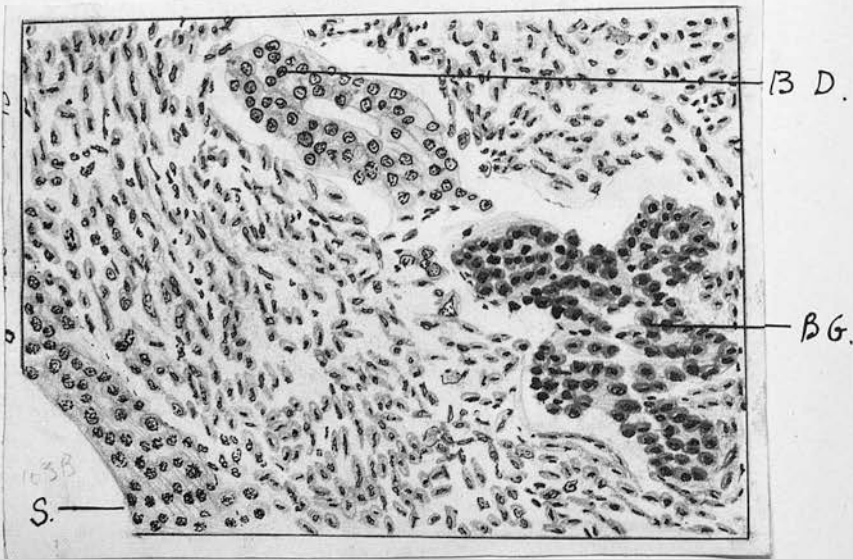


Fig. 103B

Figs. 103 A and B.

55 mm. embryo. A x 30 to show relations of sinus (s), Bartholin's gland=(B.G) Clitoris = (C), B. x 350 Area A. enlarged to show histology of Bartholin's gland and duct=(B.d.)

Figs. 104 A and B. A x 30, B x 350, Area A. enlarged to show Bartholin's duct (B.d.) entering sinus S. at (B.D.S.)

of Bartholin's gland, ventrally towards the body of the glans clitoridis. This band was not present in earlier specimens - and may possibly be the rudiment of the bulbo-cavernosus muscle (see Fig. 102).

55 mm. Embryo.

Bartholin's gland now consists of epithelial buds 4-5 in number - which possess lumina and are the acini of Bartholin's gland (see Fig. 103). These gland acini are lined by rather tall cubical or low columnar epithelial cells, which at this stage, have nuclei staining much more darkly than those of the cells lining the ducts - which latter resemble the sinus epithelium (see Fig. 104). The gland is surrounded by a slightly condensed capsule, formed of cells - more or less circularly arranged.

The longitudinal band of cells passing from the glans clitoridis to the postero-lateral sinus region is well demarcated, and the capsule of Bartholin's gland although not definitely derived from this structure, is intimately connected with it.

65 mm. Embryo.

Bartholin's duct and gland. Bartholin's duct now has a wide, well-marked lumen, lined by cubical epithelial cells resembling those lining the sinus.

The gland consists of several lumen-bearing, epithelial lined tubules. A very slight mesodermic condensation is present forming a gland capsule.

110 mm. Embryo.

110 mm. Bartholin's gland, in this specimen, con-

B.G.

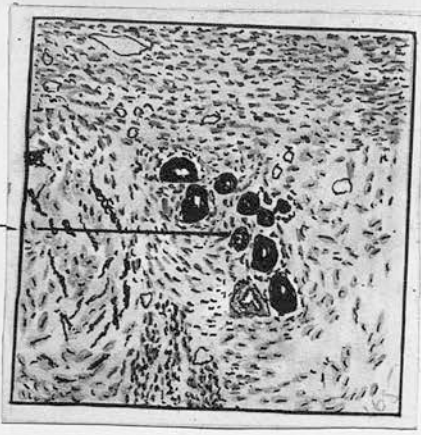


Fig. 105.

S

Fig. 106



Bd.

C.T.B.D.

Figs. 105 and 106. 135mm embryo x 80 (105) shows Bartholin's gland (B.G.) (106) shows collecting tubules of Bartholin's duct= (C.T.B.D.) S.= Sinus.

S.T.

C.D.

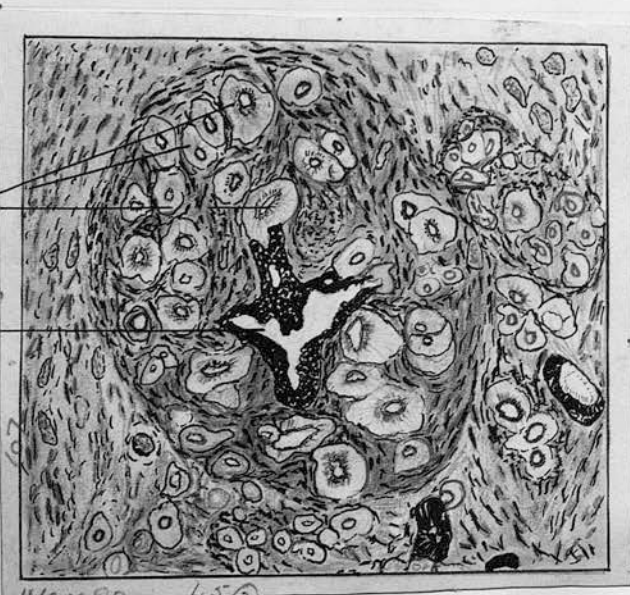


Fig. 107.

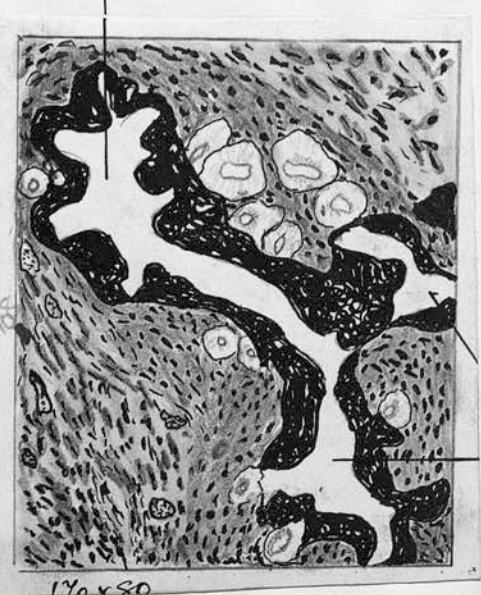


Fig. 108.

Fig. 107. 170 mm. embryo x 50 Acinus of Bartholin's gland, - secreting tubules=(S.T.) draining into central duct=(C.D).
 Fig. 108. 170 mm. embryo x 50 Collecting tubules C.T. joining together to form Bartholin's duct = (B.D.)

sists of 4-5 epithelial lined tubules, which possess well-defined lumina, and are surrounded by a layer of circularly arranged cells. These little tubes join together, and open by a common duct into Bartholin's groove.

135 mm. The gland here still consists of a group of small epithelial lined tubules. These, by now, are arranged in small groups or clusters, but definite secreting acini are not present, the tubules appearing to end distally by becoming solid. The supporting mesoderm of the gland is little differentiated. The small groups of primary tubules open into common collecting ducts, which in turn unite to form the principal duct of the gland, Bartholin's duct. This is smooth walled with a fairly wide lumen and opens into Bartholin's recess in the sinus (see Figs. 105 and 106).

170 mm. By this stage, Bartholin's gland and duct have advanced very considerably in development.

The gland now possesses a compound, racemose structure, and lies roughly parallel to the hymeneal orifice, but extending proximally along the vagina, and distally along the sinus, at some little distance from these cavities. It is enclosed in a fibro-muscular capsule, largely derived from the vaginal mesodermic condensation, but also deriving muscular bands from the perineal muscles, especially from what appears to be the ischio-cavernosus, and which lies antero-external to the gland.

The gland acini consist of groups of tubules, lined by lightly staining, rather high columnar epithelial cells. These cells have a granular or "ground glass" appearance, due to distension with mucus i.e. - the gland has attained its true secreting function. A group of these tubules each of which possess a tiny central lumen, drain by branching ducts, into a central placed collecting channel, the lumen of which is lined by low columnar or cubical darkly staining cells. The acinar groups - and indeed the individual tubules are embedded in a fine fibro-vascular network derived from the main capsule of the gland. The collecting ducts join to form Bartholin's duct which is here wide-lumened and lined by similar low, darkly staining cubical epithelium, which is irregularly heaped up in places, giving the lining membrane a slightly villous appearance (see Figs. 107 and 108).

It can be seen that the gland is now in development comparable with that found in the full term foetus, and further specimens will not therefore be described. In the work of other investigators I have found little of a controversial nature, written with regard to the development of Bartholin's gland.

Eggerth (56) discusses the origin and development of the major vestibular or Bartholin's glands. He quotes Huguier as finding the glands first in a $4\frac{1}{2}$ months embryo, while Tourneux (21 (B)) gives the stage at 44 mm.

Müller (57) - he states - finds no trace of the developing glands in a 27 mm embryo, but describes their appearance just after this date - as a solid thickening of the epithelium lining the urogenital sinus. This solid outgrowth becomes hollow and terminates distally by separating into a 5-rayed star - between the buds of which is a cellular mesenchyme growth.

Robert Meyer (31C) and Broman (58) are both quoted in this paper. They both describe a series of longitudinal, more or less constant folds in the lateral sinus wall - five in number -

According to Robert Meyer, Bartholin's duct arise from the third - while Broman describes an upper middle and lower, and derives the gland from the middle groove.

Eggerth considers that the epithelial indentations from the sinus just below the utero-vaginal junction, i.e. a 45 mm. specimen—I take it he means here those noticed in the substance of the anterior urogenital crest—may be the anlage of Skene's tubules.

Eggerth's conclusions re the developing Bartholin's gland are as follows :-

1. Human embryos from the 30-60 mm. stage present in the sinus three pairs of lateral folds extending from the ostium urogenitalis towards the entrance, or contact area - of the utero-vaginal canal and sinus.

2. Bartholin's gland is first recognised in the 30 mm. stage - arising from the middle fold near its cephalic end.

3. The development of the glands is not symmetrical on both sides.

It will be noticed that these results are strictly comparable to the ones I have just described in my own specimen - the three lateral longitudinal grooves being those which I have designated in my description as "A", "B" & "C", "B", or the middle groove, being that which gives origin to Bartholin's gland and duct.

CONCLUSION & SUMMARY

The subject of this thesis is, in its nature, so extensive and complicated, that I, at least, have found it practically impossible to avoid some confusion and repetition in the descriptions.

Therefore it seems advisable, having now reached the end of the consideration of the problems involved, to make a conclusion by summing up, as briefly as possible, the general trend of my observations.

(1). The Müllerian ducts, by their modifications, give rise to the Fallopian tubes, uterus, vagina, and vaginal surface of the hymen.

(2). The Wolffian ducts take no part in the formation of the female genital tube.

(3). The Fallopian tubes represent the upper, ununited portions of the Müllerian ducts. Accessory abdominal ostia appear to be almost the rule in the embryo.

(4). The Uterus is made from the upper portion of the fused Müllerian ducts, and the mesoderm immediately surrounding these gives rise to the uterine musculature. In its growth this latter comes to include portions of the unfused ducts-cornua.

(5). The vagina owes the origin of its upper part to the remains of the fused Müllerian ducts. Its lower part is a secondary extension from this structure (vaginal bulbs) along the posterior wall of the sinus.

(6). The Sinus, although important in early embryonic life, is completely invaginated so far as its upper part is concerned, by the developing vaginal bulbs. Its lower part remains as the vestibule. 132

(7). The hymen is produced in association with the above mentioned invagination of the upper part of the sinus. Thus its lower and outer surface is covered by the lining of the invaginated sinus, its upper surface by the cells of the vaginal bulbs.

(8). The Wolffian ducts, if persistent, should, developmentally open on or near the free edge of the hymen. Frequently, however, they acquire a secondary opening near the base of this structure by atrophy of their outer walls.

(9). The orifice of the duct of Bartholin's gland is, at first, about half way down the sinus. Its definitive position, near the base of the hymen, is the result of the invagination of the proximal portion of the sinus.

The whole of this investigation has been carried out on human material, cut, for the main part transversely,

and preserved in serial sections.

The development of the genital tract in lower animal forms appears, in many cases at least, to run on somewhat different lines, and it has seemed to me that elucidation of the developmental questions of this region, in women, can only be solved by the investigation of human material.

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THE DEVELOPMENT (prenatal) OF THE FEMALE GENITAL TUBE.

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